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ADVANCES IN TREATMENT OF ACUTE AND CHRONIC RENAL INSUFFICIENCY

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Renal insufficiency is defined for this discussion as a defect in excretory function that interferes with well-being or even places life in jeopardy. The acute insufficiencies result from more or less selective toxic or ischemic damage to tubule cells, they are usually associated with oliguria or anuria, and their course is toward recovery by cell regeneration; hence, the aim of treatment is to maintain the patient until this predictable repair has been adequately effected. In contrast, in chronic renal insufficiency, blocks and masses of nephrons have usually been destroyed beyond repair. Many patients with chronic renal insufficiency can be maintained in comfortable and useful life in spite of severe defects in renal function, but treatment is essentially palliative and the ultimate prognosis commonly grave.

The causes, lesions, courses, and therapeutic aims are different in acute and chronic renal insufficiency. In both, however, the basic principles of treatment are the same. These are, first, to reduce the load of metabolites that the kidney is called on to excrete and, second, to correct specific defects of body chemistry as they appear.

EXPERIMENTAL STUDIES

Perhaps the most significant single experimental fact is that potassium intoxication is the proximate cause of death after nephrectomy. Toxic effects of protein catabolism have been repeatedly demonstrated in experimental total and subtotal renal insufficiency, and a perverted protein metabolism may occur. I,[1] among others, have shown that high calory nonprotein diets prolong life after nephrectomy, but we have been unable to confirm claims of beneficial effects of testosterone or desoxycorticosterone.

The development of the artificial kidney by Kolff and its elaboration by others has lead to a variety of clinical and experimental studies in vividialysis. A particularly important finding of these studies is the fact that in animals that have had nephrectomy and that have been kept alive by any of these methods, severe hypertension and necrotizing vascular lesions often develop. The lesions seem to result from some poorly understood effect of renal insufficiency and are greatly intensified by hypertension. Some investigators relate the hypertension to excessive retention of sodium and water. Preliminary observations by Kolff on the distribution of sodium 24 in dogs so treated tend to support this. As Muirhead and co-workers [2] point out, however, the mechanism of this condition is still obscure, a lack of information partly attributable to technical difficulties in the precise study of water and electrolyte metabolism. At least, the fact that fluid and electrolyte overloads precipitate vascular lesions in dogs that have recently had nephrectomy [3] has the clinical implication that such overloads should be avoided in patients. The occurrence of vascular lesions in animals maintained by vividialysis has the further implication that there is little promise of indefinite arenal survival in current techniques. Lastly, the vascular lesions precipitated by renin in dogs that have had nephrectomy or in rats that have been treated with adrenal steroid materials may bear on the mechanisms that operate in clinical renal disease, in which the renal pressor system is presumably operative.

CHRONIC RENAL INSUFFICIENCY

The association of the syndrome of uremia with azotemia suggests that it results ultimately from some product or process of protein catabolism, although many symptoms of uremia could result from disturbances in electrolyte and water distribution. No "uremic toxin"—should such exist—has been demonstrated. That it is not urea is apparent from the comparison of results of dialysis of patients against baths containing urea; the clinical uremia improves, while chemical uremia is unchanged.[4]

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3. Orbison, J. L.; Christian, C. L., and Peters, E.: Studies on Experimental Hypertension and Cardiovascular Disease: I. A Method for Rapid Production of Malignant Hypertension in Bilaterally Nephrectomized Dogs, A. M. A. Arch. Path. **54**: 185-196 (Aug.) 1952.

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The etiological connotation of the term uremia is inappropriate. We have, however, done better than we knew by retaining it, since it directs attention to the therapeutic need for reducing protein catabolism to a reasonable minimum. This aim is achieved by supplying a diet adequate in calories but limited in protein, by eliminating infection, and by adding to these measures rest and reassurance.

Diet.—Protein restriction is far from new. Its recent more rigid application stems largely from the realization that nitrogen balance can be secured from diets that, like the Kempner rice diet, contain as little as 20 gm. of protein. Particular dietary schemes designed for greater palatibility and more appropriate electrolyte distribution than the rice diet have been outlined by Borst [5] and Kolff.[6] Both of these observers use fat-sugar mixtures to decrease bulk while increasing caloric supply. These mixtures are useful but tend to cause nausea and should be prescribed in cautious daily increments beginning at a level of 15 cc. four times a day between meals. The consensus is that the aim is to provide between 2,000 and 3,000 calories and a sufficient restriction of protein (40, 30, or 20 gm. daily) to achieve minimal azotemia.

Infection.—Infection stimulates protein breakdown. It can, therefore, precipitate or aggravate uremia and in the form of pyelonephritis, which is common and frequently overlooked, contributes to further renal damage. It is urgent, therefore, that infections be looked for. In this regard, the antibiotics have enormously facilitated control of chronic renal disease.

Rest and Reassurance.—Both physical activity and anxiety increase metabolic rates and catabolic loads. Rest should be generously prescribed and secured, if need be by liberal use of materials that can be metabolized, such as barbiturates, trichloroacetaldehyde (Chloral), or, terminally, paraldehyde administered orally or rectally. The opiates are to be avoided. The direction of terminal care was described well by the late Thomas Addis.[7] Recently, advantage has been taken of the knowledge that sodium lactate in doses of from about 80 to 160 mEq. of a hypertonic solution sometimes increases renal function by a margin that, small in absolute terms, is claimed to stave off uremic symptoms.[8] Our experience with this regimen is small and to date unrewarding.

Electrolytes.—Correction of specific defects in body chemistry applies principally to electrolytes. Apart from the general principle of symptomatic relief of acidosis with sodium bicarbonate and the associated general measure of alimentary phosphate withdrawal by aluminum hydroxide gels (30 cc. four times a day), the major problems in this area occur in those patients who have relatively specific and disproportionate damage to functions of electrolyte excretion. Such are the "sodium-wasters." These, without their individually determined sodium supplement, drain themselves into a state of hyponatremia and reversible uremia.[9] A related change is the syndrome of renal acidosis in which calcium loss results in osteomalacia, which is relieved by administration of alkali. These patients commonly tend also to waste potassium, sometimes to the point of distressing hypokalemia. Hypokalemia may supervene in the absence of bony lesions. One such patient was carefully studied by Earle.[10] Another, who I saw in association with Dr. William Proudfit, strikingly illustrated the range of functional dissociations in chronic renal disease. She was unable to concentrate or acidify urine or to excrete potassium at a rate much less than that of glomerular filtration, while the plasma clearances of mannitol and *p*-aminohippurate (PAH) were normal, and the maximal tubular excretory capacity (Tm_{PAH}) was only slightly depressed. Her weakness and bouts of paresis were associated with a serum potassium concentration of 2 mEq. per liter. These were relieved and a concentration of about 3 mEq. per liter maintained by supplementing the potassium in her diet with potassium salts in doses of from 100 to 200 mEq. daily. The underlying renal disease in this patient, as in many with renal acidosis, was apparently chronic pyelonephritis. Attention is drawn to this exceptional case merely to emphasize the unpredictable occurrence of disproportionate remediable defects of electrolyte excretion in some patients and the need for individualization in prescribing content of electrolytes.

As to water, azotemia creates an osmotic diuresis in which the nephrons tend to excrete a urine having the osmotic activity of plasma. This adaptation, as it is termed by Platt,[11] obligates water output so that the patient tends naturally to determine his own optimum under the stimulus of thirst. When, for any reason, he is no longer able to do this, dehydration and intensified uremia result, and fluids, usually glucose in water given parenterally, must be supplied in amounts that will maintain a urinary output of about 2 liters daily.

Dialysis.—Vividialysis is infrequently indicated in chronic renal failure. The clinical response is commonly transient and often unimpressive. Exceptions occur in patients in whom infection, trauma, or exacerbations of renal disease have precipitated recoverable uremia and, apparently, in some patients with polycystic renal disease. Merrill [4] observes that "the polyuric normotensive patient responds better (to hemodialysis) . . . than does the relatively oliguric hypertensive," and he makes note of the distressing illusory hopes that the availability of "artificial kidneys" have raised in the minds of patients and their families. No less disappointing have been press notices of kidney grafts. Such operations are properly approached primarily as an exact technical and biological study; this has been the approach of the group at Peter Bent Brigham Hospital.

Hypertension.—The syndrome of malignant hypertension may appear as a complication of chronic renal disease and may rapidly accelerate the deterioration of cardiac and renal status. When hypertension seems to be

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8. Neubauer, R. A.: Some Changing Concepts of Sodium Metabolism in Cardiac and Renal Diseases, Delaware M. J. **24**: 97-100 (April) 1952.

9. Thorn, G. W.; Koepf, G. F., and Clinton, M., Jr.: Renal Failure Simulating Adrenocortical Insufficiency, New England J. Med. **231**: 76-85, (July 20) 1944.

10. Earle, D. P.; Sherry, S.; Eichna, L. W., and Conan, N. J.: Low Potassium Syndrome Due to Defective Renal Tubular Mechanisms for Handling Potassium, Am. J. Med. **11**: 283-301 (Sept.) 1951.

11. Platt, R.: Structural and Functional Adaptation in Renal Failure, Brit. M. J. **1**: 1313-1317 (June 21) 1952; ibid. **1**: 1372-1377 (June 28) 1952.

damaging per se, as it is in these patients and in those with cardiac failure, it is now possible to reduce diastolic pressure to reasonable levels, such as 110 mm. Hg, by cautious parenteral use of hexamethonium. This treatment has the risk that undue hypotension or even normotension may precipitate total renal failure. The dangers, difficulties, complications, and essentially palliative nature of such treatment should be explained to the patient or to the family. The treatment should be begun in the hospital. The initial intramuscular dose is determined from the response of arterial pressure to an intravenous test dose given slowly. The spacing and size of subsequent doses are determined by careful, frequent observation of blood pressure, azotemia, urine volume, and side-effects since, in renal failure, the drug is excreted slowly. Such treatment is not generally recommended. It should probably be reserved for those patients whose understanding is such that they can continue self-treatment at home.

ACUTE RENAL INSUFFICIENCY

In the recent past the two major hazards to the anuric patient were fluid overloads and potassium intoxication. These dangers have not been wholly eliminated. Still, one major advance is the now widespread recognition that overinfusion is both futile and dangerous, an area of information to which Strauss,[12] among others, has contributed greatly. The consensus now is that fluid replacement should be limited to estimated losses plus from 0.5 to 1 liter of water. It is, therefore, most important to measure all the excretions.

Potassium intoxication in anuria occurs because the catabolism of 70 gm. of protein, as might occur in one day's total fast, releases 140 mEq. of nonexcretable potassium; therefore, in acute as in chronic renal disease, protein catabolism should be reduced to a minimum by the provision of at least 400 Cal. daily in the form of glucose of invert sugar. Full caloric maintenance at a level of about 2,500 Cal. is recommended by Borst [5] and Kolff.[6] This procedure is not accepted everywhere [13] and it is always difficult. Data that might unequivocally show the advantages of carbohydrate calories in excess of the recommended minimum should be made available. In the interim, the practice is to exceed the minimum whenever practical, as by the use of fat-sugar emulsions in those persons who can accept them.

Many patients require maintenance of caloric intake by intravenous routes. The problem that arises is how to give adequate calories without damaging veins or burdening the patient with fluid. In general, intravenous therapy is best conducted by a constant drip through a polythene venous catheter. It can be assumed that patients who are febrile and who have an infection require more than the minimum of 400 Cal. daily. They are probably advantageously given 40% dextrose solution through a catheter placed in the iliac or caval veins through femoral venipuncture.[14] In post-traumatic renal failure from battle wounds, Capt. Paul Teschan seems to have shown the advantage of this mode of caloric supply.

Carbohydrate rations not only tend to prevent hyperkalemia but, when deposited as glycogen, cause the storage of potassium. Insulin (1 unit to 3 gm. of dextrose) is advantageously added to the dextrose drip if hyperkalemia develops. The toxic myocardial effects of potassium can be temporarily antagonized by adding calcium gluconate in doses of from 10 to 20 gm. per 24 hours. These measures can be effective only over the course of hours or days. If anuria and hyperkalemia persist other modes of potassium elimination must be used. The two made recently available are cationic exchange resins (ammonium-sodium cycle) and vividialysis. Potassium can be removed effectively by intestinal lavage, but the effects of this on fluid and electrolyte distribution are hard to control.

As for the resins, their oral or rectal use demands careful control of sodium uptake and withdrawal. Given orally, they are not well tolerated; rectally, they are less efficient adsorbents but still can withdraw about 0.3 mEq. potassium per gram of resin. In patients with intestinal stasis, there is definite risk of impaction, so that those who need them most tolerate them least. Further advances are to be expected in this field of therapy.

The remaining alternative in those with severe hyperkalemia or serious uremia is vividialysis. It will rapidly remove potassium from the body and also nearly always elicit a dramatic clinical improvement that may be sufficient to permit the resumption of conservative management with food and fluid given orally. Conservative management without dialysis can yield a recovery rate of 80%.[15] Still, from the aspect of the patient's comfort and well-being, peritoneal dialysis by the method of Grollman [15] or hemodialysis are most useful adjuncts to treatment. Further, in those patients made severely ill by the effects of trauma and infection, as in post-traumatic anuria, conservative management is definitely ineffective and dialysis is necessary for survival.

As the kidneys may "open up," the patient's condition may continue to deteriorate for a day or two because of increasing uremia. More commonly, as diuresis increases, deterioration results from uncontrolled losses of potassium and sodium that occasionally continue for long periods.[16] Fortunately, appetite and a feeling of well-being usually begin to return at this time, so that oral maintenance and replacement become practical, although continued close supervision of clinical and chemical status is necessary. Consequently, patients with acute renal insufficiency require skilled supervision and good laboratory aids even in the phase of recovery. In brief, the management of acute renal insufficiency, particularly when it is associated with trauma and sepsis, requires an unusual amount of time, knowledge, and apparatus, all of which are justifiable because condition is essentially one from which recovery is possible.

SUMMARY AND CONCLUSIONS

Basic principles of treatment in acute and chronic renal insufficiency are similar, although the lesions, courses, and prognoses of these conditions are widely different.

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15. Grollman, A.; Turner, L. B., and McLean, J. A.: Intermittent Peritoneal Lavage in Nephrectomized Dogs and Its Application to the Human Being, A. M. A. Arch. Int. Med. **87**: 379-390 (March) 1951.
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Studies in animals indicate that the possibility of arenal survival is small and suggest that excess loads of electrolytes, notably sodium, are undesirable.

Recent advances in treatment of chronic renal disease consist principally in more rigid use of low protein diets of adequate caloric content and the availability of means of controlling infection. The flame photometer has increased the ease with which disproportionate defects in electrolyte excretion can be recognized and corrected. In contrast to its usefulness in acute renal insufficiency, vividialysis is rarely effective in uncomplicated chronic renal disease. Depressor drugs, notably hexamethonium, are occasionally recommended for the control of hypertension and cardiac failure.

Advances in treatment of acute renal failure consist principally in improved conservative management and the availability of means of vividialysis. Conservative treatment consists essentially of fluid restriction, provision of a minimum of 400 carbohydrate calories daily, and control of hyperkalemia with dextrose-insulin-calcium mixtures and, when practical, cationic resins. Those persons who are severely ill require dialysis. Trauma and infection severely impair the efficacy of conservative management. The possibility of substantial recovery from and the complex course of acute renal insufficiency make it a condition that requires skilled supervision and adequate laboratory study.

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ADVANCES IN MANAGEMENT OF THE NEPHROTIC STATE

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The nephrotic state is a well-defined clinical entity without a generally accepted name. Nephrosis, lipemic or lipoid nephrosis, the nephrotic syndrome, and other names carry with them certain implications of etiology, pathology, or prognosis that are not justified in the present state of our very limited knowledge. For simplicity, the term nephrosis will be used to designate the syndrome of proteinuria, low serum albumin, high blood lipids, and variable edema. Forty-two patients, who have been studied and treated during the past three years, form the basis of the present report. One-half of the patients were 1 to 5 years old at the onset of edema. The age of the other patients varied evenly from 6 to 50 years.

No effort was made to classify patients according to cause (glomerular nephritis or lipoid nephrosis). Although a respiratory infection often preceded the onset of nephrosis, the signs of acute glomerular nephritis were not observed and the evidence of a streptococcal origin was not convincing. Patients who first had very similar signs and urine findings have followed different courses. Some have become entirely well, while a few have had increasing hypertension, hematuria, azotemia, and, at death, lesions resembling those of chronic glomerular nephritis. Did the latter group have a different disease from the onset, or did the glomerular lesions develop at a later stage? The final diagnosis has usually been made in retrospect. Although the late development of sustained hematuria, hypertension, and azotemia has been significant of a bad prognosis, minor and variable hematuria and elevation of arterial pressure and blood urea in the early stages of the disease have been of little prognostic value.

The course, without specific treatment, is one of chronic, fluctuating edema, often modified after an infection. In a few patients, the edema is of brief duration, but it usually goes on for many months, sometimes for years. Infections are frequent, especially in the respiratory tract, the skin, and the peritoneal cavity. In the pre-antibiotic era about one in every three patients used to die of infection. This figure has been greatly reduced. In the present series, there have as yet been no deaths from infection.

The ultimate outcome of reported groups is highly variable. Spontaneous, complete remissions have occurred in as many as 32% of one group of children in whom nephrosis and nephrotic nephritis was diagnosed.[1] In an unselected group of children and adults from another hospital, only 12% of the patients recovered completely, when deaths from infection were eliminated.[2] The remaining patients showed continuing signs of renal disease. Somewhat less than 40% of patients in the published series died with uremia within five years. Better results are recorded in those series from which patients with definite hemorrhagic nephritis are excluded.

The symptomatic improvement that can be achieved with modern treatment has made the collection of a simultaneous control series very difficult. We can describe the immediate changes in the patient's course after certain forms of treatment. The question whether we have modified the ultimate prognosis is still in doubt because of the lack of comparable controls.

AIMS AND MODES OF TREATMENT

Treatment should be directed primarily toward the survival and ultimate recovery of the patient from the renal disease and secondarily toward the relief of edema and other symptomatic manifestations of the nephrotic state. Survival depends on management of intercurrent hazards, notably infection, malnutrition, and massive edema, together with the rarer complications of hyper-

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2. Rennie, J. B.: Oedematous Syndrome of Nephritis with Special Reference to Prognosis, Quart. J. Med. **16**: 21-31 (Jan.) 1947.

tensive crisis, cardiac failure, and acute exacerbations of renal insufficiency. True recovery is the cessation of activity of the renal lesion. Clinical relief of symptoms and signs may occur with residual evidences of a renal lesion or of its consequences, namely, hypertension. Edema may be worthy of therapeutic attention when it threatens the breathing reserve or makes nutrition a serious problem. Measures directed against edema should be evaluated not only for effectiveness but also for possible risks, both immediate and long-range.

Bed rest stimulates diuresis in only the mildest cases. It is apparently without effect on the outcome of the disease. In addition to its bad effect on morale, prolonged bed rest may cause undesirable shifts of fluid to the genitalia, abdomen, or chest and may predispose the patient to venous thrombosis.

A generous fluid intake is usually prescribed but is not always accepted by the patient. Anorexia may frustrate efforts to improve nutrition. Various special diets have been tried without convincing results. Restriction of sodium intake to less than 1 gm. of sodium chloride per day may be helpful, but this may also impair the total intake of food or may lead to an undesirable reduction of serum sodium concentration. Cation exchange resins have been of very limited assistance and have been poorly tolerated. The conventional diuretics are unreliable. We have not used mercurial diuretics because of the risk of serious immediate reactions and possible aggravation of the renal lesion. Concentrated human serum albumin induces a temporary diuresis in about one-half of the patients who receive 50 gm. intravenously for four or more days.[3] Whole blood may be useful in patients with marked anemia.

ROLE OF INFECTION

The control of preexisting infections and the removal of foci of infection should be undertaken only in accordance with established principles of sound practice, not in the hope of improvement of the nephrotic state.

Intercurrent infection is one of the chief causes of morbidity and death in nephrosis. The upper respiratory tract, the skin, and the peritoneal cavity seem especially vulnerable, and bacteremia is not infrequent. Prompt treatment is essential. The common infection caused by a pneumococcus or hemolytic Streptococcus is controlled with penicillin. Less common and more resistant bacteria of the gram-negative types have appeared with increasing frequency with the widespread use of antibiotics, calling for the use of penicillin plus streptomycin or a broad spectrum antibiotic in immediate treatment. Bacteriological cultures and study of sensitivity of organisms should be made at once in any serious infection.

The long-term administration of antibiotics to avoid recurrent infection has not yet been generally accepted. The replacement of the normal flora with bizarre and resistant organisms presents new problems, and the effectiveness of the prophylaxis is uncertain. We have preferred prompt treatment rather than attempts at prevention.

MODIFICATION OF RENAL LESION

Spontaneous diuresis sometimes follows an infection. Measles and vaccinia have been induced in nonimmune patients, with temporary or lasting benefit. Influenza vaccine has also been followed by improvement in some cases.[4] Nitrogen mustard has been administered with benefit to certain patients, but many undesirable effects are produced.[5] Corticotropin (ACTH), cortisone, and hydrocortisone will be considered in more detail, since their more general use warrants further consideration of their effectiveness and certain hazards.

CORTICOTROPIN, CORTISONE, OR HYDROCORTISONE

Much remains to be learned about the mechanism of action of the adrenal cortical hormones in nephrosis. In addition to the renal lesion in nephrosis with proteinuria, impaired glomerular filtration, oliguria, and sodium retention, there is evidence suggesting some aberrations of adrenal cortical function and of the metabolism of proteins and lipids. Improvement or remission of many of these evidences of the disease may occur either during or after treatment with corticotropin, cortisone, or hydrocortisone.[6]

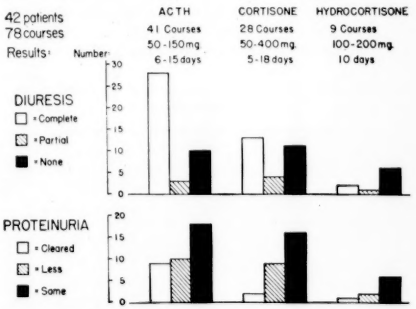

Fig. 1.—Figure shows the immediate effects of the adrenocortical hormones on edema and proteinuria of the nephrotic state. It is evident that the incidence of diuresis and clearing of proteinuria was highest in patients receiving corticotropin (ACTH).

In our series of patients, these hormones have been given in full dosage for 10 to 14 days (fig. 1) and then withdrawn abruptly. Shorter periods of administration are less likely to reach a full effect. Treatment for periods

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longer than two weeks have generally not been employed for several reasons. There seems to be a diminishing return of benefit with further treatment, if no improvement is evident after two weeks. The hazards of prolonged use of the potent adrenocortical hormones in these patients are considerable. Since we have been reluctant to administer the hormones without hospitalization and the closest observation, the cost in time and expense has been heavy. Furthermore, improvement may occur when the administration of the hormone is stopped. In contrast to prolonged treatment, brief courses are safer and easier for all concerned and offer the double chance for improvement on either treatment or withdrawal.

It is axiomatic that the optimal dosage is one that produces the desired effect with a minimum of undesirable actions. Daily dosage less than 40 mg. of corticotropin or 100 mg. of cortisone is likely to be ineffectual, even in small children. Doses of more than 100 mg. of corticotropin or 300 mg. of cortisone per day are likely to be associated with pronounced side-effects. We suggest as initial dosage in children: corticotropin, 50 mg. intramuscularly per day, divided into four equal doses; corticotropin gel, 20 units twice a day; or cortisone, 200 mg. per day, divided into four equal oral doses or given intramuscularly once a day if oral medication is refused or vomited. Hydrocortisone acetate is effective when given by mouth in dosage comparable to that of cortisone; intramuscular injection of hydrocortisone acetate is apparently less reliable. Older children and adults may be given one and one-half times these doses. If improvement fails to appear, a further course of treatment with larger doses is recommended.

Special Risks in Use of Corticotropin or Cortisone in Nephrosis

- Initial stage
  - Oliguria
  - Increased edema
  - Increased blood pressure
    - Hypertensive encephalopathy
  - Hypotonicity—low serum sodium
  - High serum potassium
  - Increase in azotemia
- Diuresis
  - Potassium depletion
  - Dehydration
  - Peripheral vascular collapse
  - Tachycardia
- Infection
  - Masking of symptoms and signs
  - Rapid spread
  - Failure of antibiotics
- Blood
  - Leukocytosis
  - Thrombosis and embolism

General agreement has not yet been reached on the relative effectiveness of corticotropin as compared with cortisone. We have usually started with a moderate dose of cortisone. If this failed, the next course of treatment was frequently with corticotropin at a somewhat more effective dosage. This approach has been one of convenience, since cortisone can be taken by mouth and the discomfort and slight risk of multiple intramuscular injections in an edematous, infection prone patient avoided. This has weighted the series in favor of corticotropin, since any further treatment may result in improvement after one or more unsuccessful attempts. The data seem to show that corticotropin is slightly more effective than cortisone, but the effects may be due to quantitative differences in the effective levels of adrenal hormones produced rather than to some undetermined qualitative difference in biological action. Repeated courses of treatment favor the opportunities for improvement in resistant cases.

SIDE-EFFECTS OF TREATMENT

The administration of large doses of these potent hormones may lead to the familiar undesirable clinical reactions. In addition to the recognized risks, there are certain unusual hazards in the treatment of patients with nephrosis (see table). When edema and effusions are massive, the further fluid retention, which occurs in the early days of treatment, may produce severe discomfort and further impairment of vital capacity. In such cases, it may be desirable to do an abdominal paracentesis before administering the hormone. Severe restriction of sodium intake is unsatisfactory, since fluid accumulates in any case, while the serum (and extracellular) sodium concentration may fall to dangerously low levels. A diet containing 3 gm. of sodium chloride per day seems to be satisfactory, in most patients.

Small increases in blood pressure are the rule during the use of corticotropin or cortisone. An occasional patient has a sharp rise of pressure, culminating in hypertensive encephalopathy if the hormone is not withheld. The increase in arterial pressure during administration of cortisone appears less than that observed with corticotropin.

Increased levels of urea in the blood are common in nephrosis, and these may rise further with the administration of the adrenocortical hormones. Such changes are usually of no clinical importance, unless the patient is already on the verge of renal insufficiency. The blood creatinine is much more useful in assessing renal functional status before and during treatment because it is only slightly affected by oliguria and increased protein catabolism.

Potassium balance may change in a rapid and unexpected manner during treatment. It is important to check the serum potassium concentration at intervals of two or three days. In the early days of treatment, the serum potassium may rise rapidly to dangerous levels. This can usually be controlled with an increased fluid intake and a reduced potassium content of the diet. As the urine volume increases during later days of treatment, the serum potassium concentration may fall below normal and call for supplements of potassium. Potassium chloride, 3 to 5 gm. per day, will usually suffice, but, during a profuse diuresis, much larger quantities may be necessary to balance the large losses in the urine.

Tachycardia, lowered blood pressure, and dehydration may appear at the end of a rapid diuresis. Extra sodium should be added to the diet, and blood or concentrated human serum albumin may be used to combat hypotension.

Infection has been a frequent and dangerous complication of treatment. Symptoms and signs of infection are often concealed by the antipyretic and anti-inflammatory actions of the adrenal cortical hormones, and a clinical flare-up is frequently observed when administration of

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the hormones is stopped. The leukocytosis that regularly develops during treatment may be misleading. The benefits of hormonal treatment may be blocked or interrupted by an infection. Routine administration of full therapeutic doses of a broad spectrum antibiotic prevents many of these hazards, but infection with resistant organisms may occur. Any new symptoms or signs should stimulate a careful search for infection. Hormone administration should be withdrawn if rapid spread of infection occurs.

Venous thrombosis and embolism may occur spontaneously in nephrosis. Since these complications may possibly be precipitated by infection and by adrenal cortical therapy, a careful watch should be maintained.

COMMENT

The improvement that follows the use of corticotropin or cortisone in nephrosis varies from complete remission to no measurable effect. Repeated courses of treatment may produce further beneficial effects. If relapse occurs after a period of improvement, another course of treatment is indicated. When remission lasts for more than six months, the outlook is good; relapse after a year's remission is rarer (fig. 2).

A much longer period of observation will be necessary to evaluate the final result, but certain conclusions can be drawn from the available data. Approximately 43% of both the adults and the children who have received corticotropin or cortisone, or both, have now been apparently well for more than one year (fig. 3). This result is encouraging, but it is only slightly better than the spontaneous outcome of some groups of patients who did not receive adrenal cortical hormones. Two additional questions arise. Are the risks of hormonal treatment justified by the results? Can we do better with any other plan of

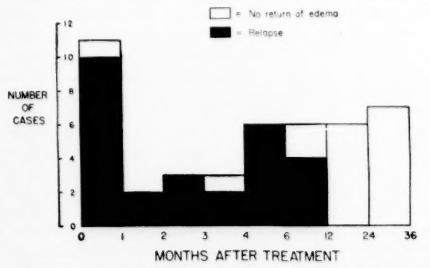

Fig. 2.—Duration of relief of edema after treatment with corticotropin (ACTH), cortisone, or hydrocortisone is shown. Edema reappeared in the first month after treatment in 23% of patients and relapses occurred in 6% during each of the next five months. Edema did not recur after it had been absent for one year.

administration of the adrenal cortical hormones? These questions are related, since the larger dosage and more prolonged treatment, which have been suggested, may well increase the incidence of undesirable hormone actions.

Severe complications and a few deaths have been reported during the administration of very large doses of corticotropin.[6c] We have preferred to use a more cautious therapeutic approach, since some patients who fail to respond to treatment recover spontaneously. If more patients are to be helped, more prolonged treatment may be helpful.[7] This approach would seem most attractive in those patients who respond to treatment with complete disappearance of signs of the renal lesion, only to relapse after the end of treatment and ultimately to progress to signs of glomerular nephritis and uremia and then to death. Insufficient data are available at this time to

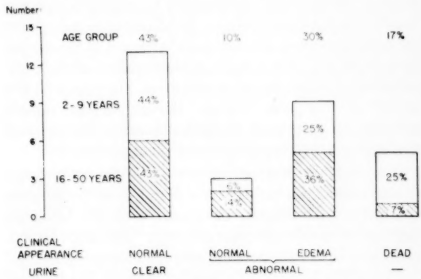

Fig. 3.—Figure shows clinical status and status of urine in patients followed for more than one year after treatment. Percentages at the top of each block are for all ages; open areas represent children and shaded areas adults. About 43% of children and adults recovered from nephrotic state after treatment.

evaluate plans for long-term treatment. Therapeutic enthusiasm should not obscure certain inevitable problems of long-term treatment, especially the cumulative hazards to the patient and the heavy burden of constant medical attention necessary for the patient's protection.

SUMMARY AND CONCLUSIONS

Observations are made on the effects of treatment of 42 children and adults in the nephrotic state. Prompt treatment has been effective in the control of intercurrent infection. Continuous administration of antibiotics for prophylaxis has not been used except during treatment with cortisone or corticotropin (ACTH).

Treatment with cortisone or corticotropin apparently shortened the nephrotic episode in certain patients. The lack of comparable controls makes it difficult to be certain whether the ultimate outcome of the whole group has been improved. One or more courses of treatment with moderate dosage of cortisone or corticotropin for two weeks has reduced or eliminated symptoms and signs of the nephrotic state in a large proportion of the patients. Repeated relapse or failure of treatment calls for some change in the plan of treatment. Larger dosage or more prolonged treatment with cortisone or corticotropin may be indicated in selected cases, but some increase in the hazards of treatment must be anticipated and controlled.

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7. Kramer, B.; Goldman, H., and Cason, L.: Treatment of the Non-edematous Nephrotic Child with ACTH, J. Pediat. **41**: 792-803 (Dec.) 1952. Merrill, A. J., and Mitchell, G. L., Jr.: Continuous ACTH Therapy of Nephrotic Syndrome in Children, Abstract from 45th Annual Meeting of the Am. Soc. for Clin. Invest. (May) 1953, p. 44. Lange, K.; Slobody, L. B., and Strang, R. H.: Serum Complement Levels as a Guide for Diagnosis and Therapy of the Nephrotic Syndrome, ibid., p. 36.

OUTLOOK FOR PATIENTS WITH GLOMERULONEPHRITIS

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Bright realized early in his studies that renal disease was a complex problem.[1] He stressed the relationship of renal dysfunction and abnormality to general edema and cardiovascular abnormalities. In addition, he recognized the development of metabolic disturbances as the disease progressed and, for a better understanding of their significance, invited the cooperation of the chemist. The results of this joint venture, though meager, anticipated by 75 years some of the biochemical findings now thoroughly appreciated by the medical profession.

The early students of diffuse nephritis realized the serious outlook for the patient suffering from the progressive form of the disease. They learned slowly, however, that there was an acute reversible type [2] that often healed, and that some of the patients with the chronic form lived and were able to work for a number of years. Bright, after a decade of study,[1b] partially reversed his earlier gloomy predictions with regard to the latter group and stated, "I believe with care its fatal effects may be kept at bay and a hazardous life may be protracted for many years." This was also the viewpoint in succeeding generations of such authorities as Johnson,[3] Bartels [4] and Roberts [5] and others.[6] Bartels and Roberts went a step further and stated that they had observed patients who had chronic parenchymatous nephritis but later recovered.

To clarify our present conceptions with regard to the course of diffuse nephritis, a group of us in Rochester made a follow-up study of a special series of 50 patients who had acute or chronic glomerulonephritis or lipoid nephrosis. We endeavored to make the diagnosis as accurate as possible and thus to avoid cases of a mixed type, which have in the past confused similar studies. Only cases of which we have records for nine and one-half years or more were included; actually some patients were observed over periods of 20 to 40 years (table 1).

The data of this follow-up study were obtained by (1) subsequent visit and examination, (2) letter from patient or patient's near relative, (3) letter from patient's home physician, (4) sometimes on change of address, through a credit bureau, or (5) statement from the municipal or state bureau of statistics in case of death in certain instances.

Periodic investigation of the individual patient included a clinical evaluation, appropriate chemical estimations of certain constituents of the blood and urine, and specific renal functional studies. These observations were frequently made during a period of hospital care and therapeutic investigation. Our chief objective has been the accumulation of significant data during the long-term course of the disease and the interpretation of their value as to the initiation of treatment and as to prognosis.

RESULTS

1. *Acute Glomerulonephritis.*—Our results in a small series of eight cases of acute glomerulonephritis with regard to age, sex, and duration of the disease confirmed previous investigations.[6b] All our patients were males, aged 11 to 63 years. Five were young adults, but three were in the sixth and seventh decades. All our patients recovered, the duration of their illnesses varying from one month to three years. Subsequent to the patients' recoveries, we observed them for from 10 to 26 years. In none was there a recurrence of the disease nor did cardiovascular alterations develop in any. In a single patient, renal disease was accompanied by hyperthyroidism, which responded satisfactorily to surgical treatment. In another patient, aged 11 years, during the first week of illness, renal function, particularly the excretion of urea, was seriously reduced, the concentration in the blood rising to 376 mg. per 100 cc. Within two weeks it had fallen to a normal level. Some years later this patient was inducted into the armed forces, served his term, and was discharged in excellent health. Our experience with these eight patients confirms a statement made by Johnson, in 1889 [7] that patients who have acute nephritis may recover in a similar manner to those who have acute bronchitis or pneumonia. Bartels, however, in 1877,[4] warned the profession that there may be fatal cases of acute nephritis, and acute fulminating cases still occur. Statistical studies carried out in recent years, both on children and on adults, indicate that a large percentage of these patients recover. The most satisfactory results appear to be in patients who receive early and adequate medical care.

2. *Lipoid Nephrosis.*—It is agreed by all that lipoid nephrosis is difficult to distinguish from glomerulonephritis with nephrotic features. Our criterion for distinguishing the former from the latter was the absence of

Read in the Symposium on Recent Advances in Nephritis before the Section on Experimental Medicine and Therapeutics at the 102nd Annual Meeting of the American Medical Association, New York, June 2, 1953.

1. (*a*) Bright, R.: Reports of Medical Cases Selected with a View of Illustrating the Symptoms and Cure of Diseases by a Reference to Morbid Anatomy, London, Longman, Rees, Orme, Brown and Green, 1827, vol. 1; (*b*) Cases and Observations, Illustrative of Renal Disease Accompanied with the Secretion of Albuminous Urine, Guy's Hosp. Rep. **1**: 338-379, 1836; (*c*) Tabular View of the Morbid Appearances in 100 Cases Connected with Albuminous Urine: With Observations, ibid. **1**: 380-400, 1836.

2. Bright, R.: Observations and 24 Cases Illustrative of Renal Disease Accompanied with the Secretion of Albuminous Urine, Memoir II, Guy's Hosp. Rep. **5**: 101-161, 1840.

3. Johnson, G.: On the Forms and Stages of Bright's Disease of the Kidneys, with Especial Reference to Diagnosis and Prognosis, Med.-Chir. Tr., London **42**: 153-164, 1859.

4. Bartels, C.: The Structural Diseases of the Kidney, and General Symptoms of Renal Affections, in Cyclopedia of the Practice of Medicine, edited by H. von Ziemssen, New York, William Wood and Company, 1877, vol. 15, pp. 1-539.

5. Roberts, W.: A Practical Treatise on Urinary and Renal Diseases, Including Urinary Deposits, ed. 4, London, Smith, Elder & Co., 1885.

6. (*a*) Loeb, R. F.: Nephritis (Bright's Disease), in Cecil, R. L.; Loeb, R. F., and others: A Textbook of Medicine, ed. 8, Philadelphia, W. B. Saunders Company, 1951, pp. 931-950. (*b*) Addis, T.: Glomerular Nephritis: Diagnosis and Treatment, New York, the Macmillan Company, 1948.

7. Johnson, G.: The Clinical History of Intermittent and Latent Albuminuria, Brit. M. J. **1**: 225-229 (Feb. 2) 1889.

diminished glomerular function. We have placed four patients in the group having lipoid nephrosis. Their ages varied from 18 to 24 years. Some data concerning patient H. M. are given in table 2. Three patients were women and one was a man. We have evidence that all four patients recovered. The duration of the disease varied in three from 3 months to 10 years; in the fourth patient we

TABLE 1.—*Type of Disease in Fifty Cases of Glomerulonephritis*

Type of Disease	No. of Cases	Age of Onset, Years	Sex	Duration of Disease, Years	Length of Follow-Up, Years
Acute glomerulonephritis...	8	11-63	M	1/12- 3	10-26
Lipoid nephrosis.....	4	18-24	1 M 3 F	1/4-20*	6-30
Chronic glomerulonephritis					
1. Patients who recovered	4	9-60	2 M 2 F	2- 8	6-20
2. Cases with nephrotic features	26	17-55	14 M 12 F	9½-41	9-41
3. Dry type.....	8	11-54	6 M 2 F	10½-27½	10½-27½

* Recovery period of less than 20 years.

TABLE 2.—*Data in a Case of Chronic Lipoid Nephrosis with Recovery in a Youth (H. M.), Aged Eighteen*

Date	Weight, Kg.	Blood Pressure, Mm. Hg	Edema, Grade	Blood: Erythrocytes, Millions per Cu. Mm.	Blood: Urea, Mg. per 100 Cc.	Blood: Serum Protein, Gm. per 100 Cc.	Urine Protein, Grade
5/15/25	..	.....	3	...	..	...	3
8/12/25*	82	120/85	4	5.5	15	4.0	3
9/29/25	58	.....	0	...	21	5.2	2
3/ 2/28	70	110/75	0	4.8	23	...	3
12/18/33†	89	125/85	0	...	32	7.9	0
4/10/38‡	..	118/70	0	...	..	...	0

* Plasma cholesterol 615 mg. per 100 cc.
† Plasma cholesterol 222 mg. per 100 cc. Hemoglobin level 17.5 gm. per 100 cc.
‡ The duration of the illness was from 3 to 8 years, following which there was no evidence of disease for 19 years. The total observation extended over 28 years.

surmise its duration was considerably less than 20 years, although the crucial tests, indicating recovery, were made at the end of that period (table 3). Frequent observations of one of these patients were made over a period of three decades and at no time following recovery were we able to reveal any renal or cardiovascular dysfunction. Murphy and associates [8] and Rennie [9] have reported similar results in some of their adult patients, and Schwarz and associates, Block and colleagues, Barness, Moll, and Janeway,[10] and Riley in certain children.

3. *Chronic Glomerulonephritis.*—The group of patients with chronic glomerulonephritis is of great interest for many reasons. Of the total of 38 patients, 4 recovered, and the life of 34 patients, who had persistent evidence of the disease, was prolonged for from 9½ [11] to 41 years. There have been reports of similar single cases from time to time in the literature. Recovery from chronic glomerulonephritis is indeed a rare event (table 3). One is not greatly surprised that it occurred in a girl and a boy 9 and 16 years of age. Its occurrence in 2 adults, aged 56 and 60, is exceptional, however. One of the latter was also suffering from hyperthyroidism, which responded to surgical treatment (partial thyroidectomy). The other, a 56-year-old man (P. K.), represented really an extraordinary case of nephritis (Bright's disease). During the first year of his illness, hematuria and anasarca were present, and edema was accompanied by a large excretion of protein in the urine, hypoproteinemia, and hypercholesteremia; renal insufficiency was also considerable, the blood creatinine rising to a concentration of 4.2 mg. in 100 cc. and the urea clearance falling to 11 cc.; hypertension and a severe vascular retinitis were present and for a short period pulmonary edema and mental confusion were striking symptoms. He slowly improved during the next 10 months and then returned to work. Renal insufficiency continued for another year. Six years after onset, evidence of renal and vascular disease was lacking (table 4). Six years later the patient died suddenly in a berth of a Pullman sleeping car. Coronary disease appeared to be the most likely cause.

The presence of edema in chronic glomerulonephritis is a difficult and challenging problem. Earlier investigators considered it as primarily renal in origin, but now it is known that general metabolic factors may also play a role. An obvious difficulty in the management of edema is the presence of renal damage. A physician naturally hesitates

TABLE 3.—*Data in Sixteen Cases of Glomerulonephritis with Recovery*

Type of Disease	No. of Cases	Age of Onset, Years	Sex	Duration of Disease, Years	Length of Follow-Up, Years
Acute glomerulonephritis...	8	11-63	M	1/12- 3	10-26
Lipoid nephrosis.....	4	18-24	1 M 3 F	1/4-20*	6*-30
Chronic glomerulonephritis	4	9-60	2 M 2 F	2- 8†	6†-20

* The recovery period for this patient, L. C., was less than 20 years. The subsequent follow-up period was more than 6 years.
† The recovery period for this patient, P. K., was less than 8 years.

TABLE 4.—*Data in a Case of Chronic Glomerulonephritis* with Recovery in a Fifty-Six-Year-Old Man (P. K.)*

Date	Edema, Grade	Blood Pressure, Mm. Hg	Retinitis, Grade	Blood: Hemoglobin, Gm. per 100 Cc.	Blood: Urea, Mg. per 100 Cc.	Urine: Protein, Grade	Urine: Erythrocytes, Grade
1/ 5/38†	2	190/110	4	12.5	68	4	1
1/16/38	2	215/110	..	....	..	4	2
1/18/38	1‡	205/125	..	10.6	70	4	0
6/16/38	0	120/80	?	10.0	64	2	1
10/27/38	0	150/105	?	13.5	56	3	1
10/25/39§	0	135/110	0	14.2	48	2	1
4/28/43	0	140/90	0	....	..	0	0

* Onset of disease March, 1937.
† On 1/8/38 the serum protein level was 4.3 gm. per 100 cc.
‡ Patient's weight decreased 8 lb. (3.6 kg.) in 12 days.
§ On 10/27/39 the serum protein level was 6.4 gm. per 100 cc.

to stimulate a diseased organ in order to produce diuresis. Nevertheless we believe definite progress has been made in the treatment of the nephrotic syndrome in glomerulonephritis. This advance is due, in great part, to the application of biochemical studies to these patients. In our

8. Murphy, F. D.; Warfield, L. M.; Grill, J., and Annis, E. R.: Lipoid Nephrosis: A Study of Nine Patients, with Special Reference to Those Observed Over a Long Period, Arch. Int. Med. **62**: 355-376 (Sept.) 1938.
9. Rennie, J. B.: The Oedematous Syndrome of Nephritis with Special Reference to Prognosis, Quart J. Med. **16**: 21-31 (Jan.) 1947.
10. Barness, L. A.; Moll, G. H., and Janeway, C. A.: Nephrotic Syndrome: I. Natural History of the Disease, Pediatrics **5**: 486-503 (March) 1950.
11. Wooding, K. R.; Keith, N. M., and Edwards, J. E.: Chronic Glomerulonephritis: Report of a Case Followed from Onset to Termination During a Period of Nine Years, M. Clin. North America **35**: 1167-1183 (July) 1951.

series of 26 cases, the relatively long and favorable course of a decade or more has afforded a unique opportunity for the study of various factors and for appraisal of treatment. In 14 patients, the advent of diuresis led to a loss of 20 lb. (9.1 kg.) or more in weight, the range being 23 to 82 lb. (10.4 to 37.2 kg.). In 12 patients, the loss of weight varied from a few to 18 lb. (8.2 kg.). In patient

TABLE 5.—*Data in a Case of Chronic Glomerulonephritis with Excessive Edema* in a Thirty-Year-Old Man (P. M.)*

Date	Weight, Kg.	Blood Pressure, Mm. Hg	Edema, Grade	Blood: Hemoglobin, Gm. per 100 Cc.	Blood: Urea, Mg. per 100 Cc.	Blood: Plasma Cholesterol, Mg. per 100 Cc.	Urine Protein, Grade
5/../29	..	......	3	....	....	....	2
11/18/29	71	130/108	4	10.4	80	552	3
12/18/29	44	120/80	2	7.3	10	...	1
2/ 3/30	44.5	110/90	0	11.2	25	...	1
12/30/30†	63	115/85	1	12.6	50	725	4
10/20/33‡	59	125/90	0	15.9	22	327	3
7/ 6/44§	..	220/140	..	....	..	....	4

* The patient's normal weight was 62 kg.
† Serum protein 4.1 gm. per 100 cc.
‡ Urea clearance 67 cc.; serum protein 5.0 per 100 cc.
§ The patient died of uremia after a course of 15 years.

TABLE 6.—*Metabolic Changes in a Case of Chronic Glomerulonephritis with Excessive Edema (Patient P. M.)*

Date	Weight,* Kg.	Edema, Grade	Blood: Urea, Mg. per 100 Cc.	Blood: Serum Protein, Gm. per 100 Cc.	Blood: Plasma Cholesterol, Mg. per 100 Cc.
11/18/29	71.2	4	80	3.6	552
12/18/29	44.2	2	10	...	...
12/24/29	37.0	0	..	...	...
1/ 7/30	39.8	0	36	4.7	255
1/23/30	43.2	0	24	5.4	286
2/ 3/30	44.5	0	25	...	...

* The patient's estimated normal weight was 62.1 kg.

P. M. (table 5) the loss of 75 lb. (34.0 kg.) during the diuretic period led to some interesting metabolic and therapeutic problems. At the termination of diuresis, the patient weighed 81½ lb. (37.0 kg.), and his appearance reminded one of the starving persons rescued from Germany at the end of World War II. Thus, in this patient, we have striking objective evidence of general wasting of the tissues of the body and from our laboratory study, chemical evidence of disturbances of the metabolism of water, mineral salts, protein, and fat (patient P. M., table 6). Farr and others have previously noted this wasting of the body tissues in the nephrotic syndrome. During the immediate recovery period, patient P. M. ate well and gained in weight without recurrence of edema. On subsequent visits to Rochester during the next 11 months, his weight and appearance were normal with exception of a trace of dependent edema. His renal function continued to be slightly impaired and the serum proteins were still decreased. For the next 13 years, until near the time of his death from uremia, the patient was free from edema and carried on his usual manual work. Surely our experience with this patient suggests further possibilities for the future investigation of metabolic problems in nephritic edema.

Since the recognition of renal edema by Bright, numerous cases have been reported in which there is a periodicity in its appearance. Addis has reported a series of these cases with recurring episodes of edema and observed that during the edema-free period there may be an absence of proteinuria and hypoproteinemia. We have observed seven such cases in the present series and recorded detailed findings in the urine and blood of patient E. R. (table 7). In this patient, three periods of edema were noted, the first being recorded in his previous history and the second, of a year's duration, in 1938. This was succeeded by a remission of a year and one-half. There then followed the third recurrence of edema, which persisted for four to six years. The edema receded in 1946, and there has been no recurrence up to the present time, a period of seven years. These and similar cases naturally raise many questions with regard to the mechanisms involved. Further study, for example, might give us an insight into the problems of proteinuria and alterations in the proteins and fats of the blood. The periodic occurrence of edema also warns the physician to consider it in the prognosis of the individual patient.

At this point a specific diagnostic problem should be considered. Daugherty and Baggenstoss [12] in 1950 reported a small series of cases characterized by glomerulonephritis, edema, and arthritis. This condition probably belongs to the general group of conditions of which lupus erythematosus is a type. During the nephrotic stage such cases are difficult to distinguish from many of the present series of cases, as we have learned, much to our sorrow. The importance of the recognition of these cases arises from the fact that prognosis up to this date has been very serious, with a rapid course leading to a fatal end.

TABLE 7.—*Data in a Case of Chronic Glomerulonephritis with Recurring Edema and Hypoproteinemia in a Patient (E. R.) Aged Thirty-Three*

Data in Period 2, of 1 Year, 1938

Stage of Period	Edema, Grade	Blood: Serum Protein, Gm. per 100 Cc.	Blood: Serum Albumin, Gm. per 100 Cc.	Blood: Plasma Cholesterol, Mg. per 100 Cc.	Urine: Protein Grade	Urine: Protein Daily, Gm.
Onset	3	4.0	2.2	792	4	..
Interim	1	3.2	...	...	4	..
End	0	7.5	...	...	0	..

Interval 1½ Years

Data in Period 3, of 4 to 6 Years, 1940-1946

Onset	3	3.9	2.0	...	4	..
Interim	2	3.0	1.6	536*	4†	38†
End	0	7.3	5.1	240	0	..

* Total lipoids 1.5 gm. per 100 cc.
† Concentration of protein 2.4 gm. per 100 cc.

The later course of chronic glomerulonephritis, after subsidence of edema, has generally been accepted to include a latent period of varying length, which is followed by a period of cardiovascular involvement and progressive uremia. Our case C. A.[11] gives a typical example of such a course. Addis in particular considered this course to be the rule. With more detailed observations during an extended follow-up period, as in this series, we have noted

12. Daugherty, G. W., and Baggenstoss, A. H.: Syndrome Characterized by Glomerulonephritis and Arthritis: Libman-Sacks Disease with Predominantly Renal Involvement, Arch. Int. Med. **85**: 900-923 (June) 1950.

several exceptions. Our attention was drawn to the possible rapid development of diffuse arteriolar disease in 1939. Wagener and one of us (N. M. K.) at that time described the case of a young man, aged 17 years, in which the sequence of events, over a period of five years were as follows: (1) an initial period of six months, during which edema and proteinuria predominated; (2) a period of almost five years of good health, accompanied by proteinuria; and (3) a short terminal period of six weeks, characterized by severe hypertensive disease and renal insufficiency. We interpreted these terminal events as indicative of an acute diffuse arteriolar disease superimposed on a slowly contracting kidney with chronic glomerulonephritis. Necropsy confirmed this clinical conception. Since this experience we have observed the incidence of acute hypertensive episodes in several cases of chronic glomerulonephritis, not only in the terminal phase but at other times during its course. We have seen them subside without specific treatment (for example, patient P. K., table 4). Such experiences emphasize the fact that hypertension may be a reversible process during the course of chronic as well as acute glomerulonephritis.

A different type of hypertensive disease developed in one patient (A. K.) of this series. Our records of her case extend over a period of 30 years. When she was 22 years of age, general anasarca, renal insufficiency, and hypertension developed, which after three months responded to hospital treatment; during hospitalization the patient lost 40 lb. (18.1 kg.). In the next seven years the patient appeared to be in normal health except for a persistent trace of protein in the urine. Eleven years later, or 19 years after the subsidence of her initial anasarca, hypertension was discovered for the second time. To all intents and purposes she has continued to have moderate, benign essential hypertension for the last 12 years, with her general health and renal function remaining satisfactory.

In our eight cases of chronic glomerulonephritis in which edema was minor in degree or absent throughout, the latent stage of the disease varied from a few to 20 years. Another patient has been in a latent phase for 22 years; at 53 years of age, she was healthy in every way, except for the presence of a trace of protein in the urine. Five patients passed into the commoner terminal phase of hypertensive disease and uremia.

In two patients essential hypertension developed without distinct renal insufficiency. One of these, patient S. H., later proved to be of exceptional interest and data concerning him were reported in detail by Mulmed, Baggenstoss, and Burchell in 1949. Briefly, his story was as follows. In April, 1926, when he was 9 years of age, acute glomerulonephritis developed. After subsidence of the acute stage, he continued to have a considerable amount of protein in the urine, but hypertension did not develop until 10 years later, in 1936. From that date until his admission to the Mayo Clinic, in May, 1946, hypertension and proteinuria were always present when he was medically examined. At our examination, 20 years after the onset of the disease, the patient was suffering from diffuse arteriolar disease with active retinitis, seen in cases of group 3 (table 8). Bilateral supradiaphragmatic and infradiaphragmatic sympathectomy was performed, and at the time of each operation a satisfactory exploration and biopsy of each kidney were made. The surgeon described them as grossly normal in size and shape. The histological picture of the kidneys was that observed in cases of essential hypertension of the benign type with no evidence of glomerulonephritis. The patient had a favorable immediate response to sympathectomy, with a lowering of blood pressure, especially when he stood upon his feet. During the next five years the patient continued to work, his blood pressure usually measuring systolic 160 to 165, diastolic 120 to 130 mm. Hg. There was no recurrence of the retinitis, and in spite of continued grade 2 proteinuria, his renal function otherwise remained normal.

Our attention was directed in 1944 to a distinctly different and infrequent course of events in chronic glomerulonephritis. In a series of three cases, the patients sought medical advice because of hypertensive cardiovascular disease of several years' duration.[13] Because of the failure of edema to disappear when the first patient was given routine treatment for myocardial failure, urinary and blood chemical studies were instituted, which revealed the presence of lipoid nephrotic features. In this patient the nephrotic syndrome later disappeared. The events recorded in these cases support the conception of Schroeder that some cases in which essential hypertension has developed are primarily cases of chronic glomerulonephritis.

TABLE 8.—*Data in a Case of Chronic Glomerulonephritis with Later Diffuse Arteriolar Disease with Hypertension In a Nine-Year-Old Boy* (S. H.)*

Date	Edema, Grade	Blood Pressure, Mm. Hg	Retinitis, Grade	Blood: Hemoglobin, Gm. per 100 Cc.	Blood: Urea, Mg. per 100 Cc.	Urine: Protein, Grade	Urine: Erythrocytes, Grade
4/../26	1	120/70	..	....	140	3	3
../../28	0	.....	..	....	....	3	1
../../35	0	.....	..	....	....	3	0
../../36	0	210/120	..	....	....	..	..
5/27/46	0	215/155	3	15.3	264	2	0
7/18/46‡	0	120/90	1	11.2	328	2	0
10/10/46	0	150/112	0	11.9	348	2	1
8/30/51	0	164/128	0	14.5	18	2	0

* The case was reported by Mulmed, Baggenstoss, and Burchell.
† Urea clearance (standard) 40 cc. per minute.
‡ On 6/24/46 and 7/6/46 extensive supradiaphragmatic and infradiaphragmatic sympathectomies were done, on the right and left sides, respectively.
§ Urea clearance (maximal) 139 cc. per minute.
¶ Urea clearance (standard) 55 cc. per minute.

Two important developments have followed the application of renal functional studies to clinical medicine. The first is of diagnostic significance. By aid of these studies, renal insufficiency has been discovered in many more patients and in a greater variety of disease conditions than before their use was instituted. Diagnosis of an obscure uremia, either acute or chronic, has first been made possible by the simple estimation of the concentration of urea or creatinine in the blood. In the second place, renal functional studies are of prognostic value during the course of the nephrotic syndrome, as mentioned previously, and also during other phases of chronic nephritis. Those of us whose work over the years has included the care of patients with chronic uremia recall how often we were surprised at the length of time some of these patients

13. Daugherty, G. W.; Baggenstoss, A. H., and Keith, N. M.: Atypical Chronic Glomerulonephritis: Report of Cases, Minnesota Med. **29**: 1218-1229 (Dec.) 1946.

could carry on comfortably.[6a] Such patients reveal a remarkable adaptation of their tissues to very abnormal metabolic conditions.

COMMENT

A review of the natural history of nephritis in this study reveals a variety of courses. The long duration of a satisfactory existence in some of our patients made the follow-up problem much less depressing than anticipated. Acute glomerulonephritis is frequently a self-limiting disease,

TABLE 9.—*Time Between Onset and Healing of Glomerular Nephritis**

Duration of Disease, Years	No. of Cases	Percentage of Total
0.5	21	23.9
1.0	27	30.7
1.5	12	13.6
2.0	12	13.6
3.0	5	5.7
4.0	2	2.3
5.0	2	2.3
6.0	2	2.3
6.0 to 10.0	5	5.7

* Addis.[6b]

seldom recurs, and does not seem necessarily to increase the susceptibility of the patient to subsequent chronic cardiovascular lesions. Recovery from the syndrome of chronic lipoid nephrosis takes place in a small but significant number of cases. A rare patient with both the edematous and dry type of chronic glomerulonephritis may recover. Addis' experience with late recovery in acute glomerulonephritis is encouraging. In 1931 he reported data on a few patients who recovered after the disease had persisted for five years; in 1948 he lengthened this possible period to 10 years [6b] (table 9). Our own results and those of others support the viewpoint that lipoid nephrosis and chronic glomerulonephritis may run a protracted course of one to several decades (table 10). The problem of edema is still a stubborn one and has perhaps stimulated as much clinical investigation as any one phase of the disease. Nevertheless the proper use of diets, particularly the control of the intake of sodium chloride and protein, the intelligent use of diuretics and expanders of plasma, the induction of peritoneal and pleural paracenteses, and lately the introduction of cation exchange resins and of corticotropin and cortisone have all proved of therapeutic value. Further study of the antidiuretic substances (the sodium-retaining corticoids of human urine) isolated from the urine of these patients by Luetscher and Deming [14] should offer fruitful results.

Study of the occurrence of hypertension during the course of glomerulonephritis began with Bright and has continued unabated up to the present time. Bright's suggestion that hypertension might exist in chronic diffuse nephritis arose from his studies of the heart when he examined the morbid appearances in 100 of his cases. The chief structural changes in the hearts in 52 cases consisted chiefly of hypertrophy. After those hearts with disease of the cardiac valves and coats of the aorta were omitted, there remained 22 cases of marked hypertrophy, generally affecting the left ventricle. This led him to look for some less local cause for the unusual efforts to which the heart had been impelled. He considered the two readiest solutions to be either that the altered quality of the blood affords unwonted stimulus to the heart immediately or that it so affects the minute and capillary circulation as to render greater action necessary to force the blood through the distant subdivisions of the vascular system.

It has long been accepted that there is an acute and a chronic type of hypertension. The former type is observed often in acute glomerulonephritis, but it is now recognized as also occurring during the course of chronic glomerulonephritis. It may subside and may recur. A serious form is frequently associated with the terminal uremic picture. Therapeutic trial of surgical sympathectomy has revealed amelioration in a few patients, as shown by Persike and co-workers [15] and in our patient S. H., reported by Mulmed and associates. Benefit has also followed the use of hexamethonium compounds. Since their hypotensive action is due to effects on the sympathetic ganglia, their therapeutic effectiveness again emphasizes the possible role played by the sympathetic nervous system in renal hypertension. A long-continued benign hypertension is also observed in chronic glomerulonephritis as in our patients A. K. and S. H. The variations of hypertension in chronic glomerulonephritis, in regard to time of onset, course, and severity, raise speculation as to its etiology and suggest multiple causative factors.

The present follow-up study emphasizes anew the astuteness of Bright in recognizing the important interrelationships between the occurrence of edema, cardiovascular alterations, certain metabolic phenomena, and renal dysfunction. We think it is of some interest that the significance of these same factors has been pointed out by

TABLE 10.—*Duration of Persistent Chronic Glomerulonephritis in Thirty-Four Cases Including Edematous and Dry Types*

Duration, Years	No. of Cases	Mean Age at Onset, Yr.	Males	Females
Patients Living Last Report				
11-15	6	33.7	4	2
15-20	3	33.2	2	1
20-25	3	31.2	2	1
25-30	3	15.5	1	2
30+	1	22.5	0	1
Total	16	29.0	9	7
Patients Dead Last Report				
9-15	9	29.6	7	2
15-20	6	32.8	3	3
20-25	2	35.0	1	1
41	1	17.5	0	1
Total	18	30.6	11	7

several observers in the glomerulonephritis associated with toxemia of pregnancy. Our experience in this study has increased our admiration for Bright's basic contributions to the various problems that may arise during the course of glomerulonephritis. Subsequent advances in our knowledge regarding the disease are largely the result of physiological, biochemical, bacteriological and pathological investigations, instituted during the various phases, first described 115 years ago.

14. Luetscher, J. A., Jr., and Deming, Q. B.: Treatment of Nephrosis with Cortisone, J. Clin. Invest. **29**: 1576-1587 (Dec.) 1950.

15. Persike, E. C., and others: Surgical Treatment for Hypertensive Complications of Advanced Renal Disease, Arch. Int. Med. **83**: 348-354 (March) 1949.

SUMMARY

The outlook for the patient who has acute glomerulonephritis is usually good, in regard to both recovery and future health. In contrast, the outlook in lipoid nephrosis and chronic glomerulonephritis is often serious. Our long-term study reveals that a rare patient with either of these diseases recovers, and a considerable number may have a satisfactory course for one or more decades. The application of modern renal function tests has proved of distinct help in their management. The present therapeutic measures available to combat edema appear to be more effective than those employed in the past, and therapy directed to the sympathetic nervous system offers promise of alleviation of hypertension.

CLINICAL APPLICATION OF CURRENT TESTS OF RENAL FUNCTION

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Recent advances in renal physiology and methodology make it possible to assess accurately and quantitatively the discrete excretory functions of the kidney.[1] The functions subject to quantitative measurement are the rate of glomerular filtration, renal blood flow, maximal tubular excretory capacity, and maximal tubular reabsorptive capacity.

The rate of glomerular filtration is measured by means of the clearance of inulin, i. e., the amount excreted per minute divided by the plasma concentration represented by the clearance formula UV/P. Since inulin is filtered at the glomerulus and is neither reabsorbed nor excreted by the tubules, the simple clearance calculation indicates the amount of filtrate formed. The mean normal rate of glomerular filtration is 130 cc. per minute.

The renal blood flow is measured by means of the clearance of *p*-aminohippurate. Since this substance is completely removed from the renal arterial blood during one circulation through the kidneys, its clearance is identical with the rate at which the blood itself is circulated through the kidneys. The mean normal value for renal blood flow is 1,200 cc. per minute.

The maximal tubular excretory capacity represents the actual amount of functioning tubular tissue. When the plasma concentration of *p*-aminohippurate (or iodopyracet [Diodrast]) is raised above the critical level, the tubular excretory mechanism becomes saturated and excretes this substance at a maximal rate. It is designated as Tm, and the mean normal value for *p*-aminohippurate is about 80 mg. per minute.

The maximal tubular reaborptive capacity is an index of the reabsorptive capacity of those tubules supplied with glomerular filtrate. As the plasma glucose level is raised by constant infusion, a point is reached at which the tubular reabsorption of glucose proceeds at a maximal rate; if the plasma glucose is further elevated, glucose filtered in excess of this maximal rate of reabsorption passes into the urine. The mean normal value for the maximal reabsorptive capacity of the tubules as measured by glucose reabsorption is 400 mg. per minute.

These methods have not as yet been sufficiently simplified to make them practicable for routine use. They are, however, of inestimable value when a precise quantitative estimate of individual renal excretory function is desirable. In the practical and routine application of kidney function tests, we are forced by expediency to use qualitative and semiquantitative measurements. This will be so until quantitative measurements of the discrete renal functions are feasible. The tests commonly used now are urea clearance, blood urea, concentrating capacity, dye excretion, and pyelography.

UREA CLEARANCE

Urea is filtered through the glomerulus at the same rate as inulin, but it is reabsorbed by the tubules to a significant extent. The value of the urea clearance, therefore, must be lower than that of the inulin clearance; the difference is quantitatively related to the amount of urea reabsorbed. Data on the absolute urea clearance (fig. 1) show that there is a progressive increase in the urea clearance as the urine flow increases up to 1.5 cc. per minute; the inulin clearance is not influenced by the rate of urine flow. The effect of urine flow is, however, slight when it is between 1.5 and 12 cc. per minute, and the effect of urine flow in this range on the urea clearance may be disregarded in utilizing the clearance of urea as an index of renal function. Urea clearances obtained at urine flows below 1.5 cc. per minute are depressed by factors such as dehydration and lowered filtration rate, which result in values that do not represent the true rate at which the kidneys are capable of clearing urea from the blood and that are, therefore, not acceptable as an index or renal function. When the urine flow is between 1.5 and 12 cc. per minute, the mean value for urea clearance is about 70 cc. per minute per 1.73 square meters.

Since the urea clearance varies closely with the rate of glomerular filtration, both are decreased by the same factors, namely, dynamic and reversible changes in intraglomerular pressure induced by changes in the tone of the afferent and efferent arterioles, organic and irreversible obliteration of the glomerular bed, organic and irreversible changes in the preglomerular arteries and arterioles, and congestive heart failure. The determination of urea clearance should be made when the urine flow is either constant or falling, since, during a period of increasing diuresis, exaggerated and falsely high urea clearance values may be obtained.

The urea clearance, then, is an expression of the combined excretory functions of filtration and reabsorption. In the normal and under conditions of high urine flow,

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Read in the Symposium on Recent Advances in Nephritis before the Section on Experimental Medicine and Therapeutics at the 102nd Annual Meeting of the American Medical Association, New York, June 2, 1953.

1. Smith, H. W.: The Kidney: Structure and Function in Health and Disease, New York, Oxford University Press, 1951. Bradley, S. E.: The Pathologic Physiology of Uremia in Chronic Bright's Disease, American Lecture Series, Springfield, Ill., Charles C Thomas, Publisher, 1948.

the urea clearance is 65% of the simultaneously determinded inulin clearance indicating that, in its passage down the tubules, 35% of the filtered urea is reabsorbed. In advanced renal insufficiency, this figure may increase to 90% and indicate that, in this circumstance only 10% of the filtered urea is reabsorbed. This fact leads to the conclusion that reduction in urea clearance and consequent increase in blood urea in renal disease are due to a diminished rate of glomerular filtration of urea and not to increase tubular reabsorption. In spite of its complex mechanism of excretion, the clearance of urea in renal disease may be used for clinical purposes as analogous to measurement of the filtration rate.

Since the clearance technique for any substance is largely dependent on accurate timing and complete collection of urine, specimens must be collected by catheterization of the bladder. It is sufficient to collect two 30 minute urine specimens, with a single blood sample at the midpoint.

BLOOD UREA

If nitrogen and water balance are constant, blood urea concentration varies inversely with the urea clearance. With diminution in the urea clearance, there is a proportional increase in the level of the blood urea. In figure 2 is presented evidence that in both hypertensive disease and diffuse glomerulonephritis there is an inverse linear relationship between the blood urea concentration and the urea clearance. It will be noted that, from the very first decrease in the rate of urea clearance, there is an accompanying increase in the level of the blood urea.

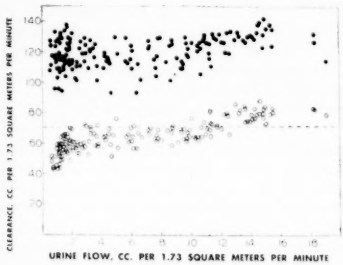

Fig. 1.—186 simultaneous inulin and urea observations in normal persons made during falling or constant urine flows. Dotted horizontal line represents mean plasma urea clearance in normal persons (70.5 cc. per minute); black dots represent inulin clearance; white dots represent urea clearance.

It cannot be accepted that the blood urea concentration rises above "normal" value only after the urea clearance has fallen to 40% of its normal value, suggesting that 60% of the renal parenchyma must be destroyed before there is an abnormal accumulation of urea in the blood. In nitrogen equilibrium, the blood urea rises from the first reduction in the urea clearance. Basis for misconception on this point is found in the following facts. (*a*) The accepted "normal" upper figure for the blood urea is 40 mg. per 100 cc.; actually the average value of a normal subject on ordinary protein diet and water intake is between 15 and 20 mg. per 100 cc. If this fact is ignored, significant minimal increase in the level of the blood urea may be overlooked. (*b*) Variations in nitrogen and water balance may significantly vary the level of the blood urea independently of the rate of urea clearance. It is possible to alter significantly the level of the blood urea by varying the protein intake; the value of the urea clearance remains unchanged (fig. 3). Since patients with renal disease frequently have disturbances in nitrogen and water balance occasioned by anorexia, vomiting, and diarrhea, it may be expected that the level of blood urea will show great variations. These variations may obscure the true relationship between rate of urea clearance and level of blood urea. (*c*) Since the urea clearance is directly related to the rate of glomerular filtration, the same factors that cause variations in the filtration rate vary the rate of the clearance of urea. The blood urea concentration may further increase as a result of decreased urea clearance occasioned by the onset of congestive heart failure in the course of renal disease. Thus, the acceptance of 40 mg. per 100 cc. as the upper limit of normal blood urea concentration and the great variations that occur in its level as a result of disturbances such as nitrogen and water imbalance and congestive heart failure have obscured the true physiological relationship between the blood urea and the urea clearance.

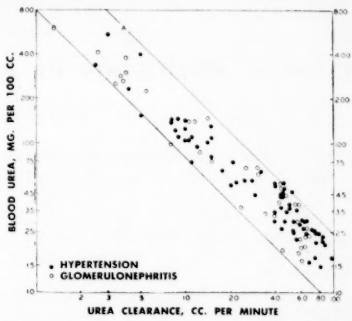

Fig. 2.—Relationship of blood urea concentration to rate of urea clearance in 103 observations in patients with hypertension and glomerulonephritis (urine flows above 1.5 cc. per minute).

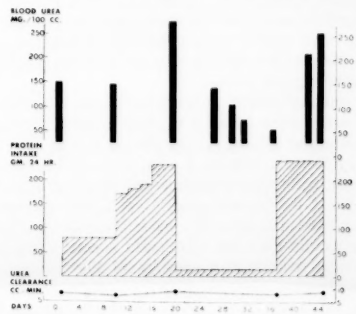

Fig. 3.—Variations in the concentration of blood urea induced by changing the protein intake in a patient with advanced renal insufficiency; urea clearance and 24 hour urine output remained constant throughout period of observation.

It is difficult to place certain prognostic significance on the level of the blood urea alone. Since the level of blood urea varies with changes in the rate of glomerular filtration, nitrogen balance, and water balance, all of which may vary independently of the renal disease, it is hazardous to attempt to use the level of the blood urea as an aid in evaluating the extent of renal functional impairment unless its abnormal accumulation is known to be solely the result of functional changes resulting from the intrinsic renal disease. Even if extrarenal factors are reasonably constant, the prognostic significance of the actual level of blood urea concentration depends on whether the intrinsic renal lesion is acute and reversible or chronic and irreversible.

MAXIMAL CONCENTRATING CAPACITY

The measure of maximal concentrating capacity is an index of the kidney's ability to excrete the maximum amount of urinary solids in the smallest amount of water. Normally the kidney is able to excrete urine containing varying amounts of solids as concentrated urine hypertonic to the blood or dilute urine hypotonic to the blood. The total amount of urinary solids can be measured by freezing point depression, surface tension, refractometry, or, for clinical purposes, the specific gravity. The specific gravity of the urine is an additive function of the concentration of its individual solutes. The urinometer measures the specific gravity of the urine and is a simple and adequate method for determining the concentration of the total urinary solids. If a large portion of the renal parenchyma is destroyed by disease, the kidneys lose their ability to vary the amount of solids in the urine, and the maximal concentrating power is decreased; a point is finally reached at which all urine excreted contains a relatively constant amount of total solids. When concentrating power has been lost, the urinary specific gravity is fixed at about 1.010. Normal kidneys can elaborate a urine with a specific gravity of at least 1.024.

Throughout the greater part of the course of hypertensive disease, the water and electrolyte reabsorptive capacity of the tubules is unimpaired, and, consequently, the maximal concentrating capacity of the kidneys is normal. It is not until late in the disease that the maximal specific gravity obtainable falls to values below 1.024; it finally becomes fixed at about 1.010. The reduction in maximal concentrating capacity late in the disease is due to loss of functioning nephrons. The mechanisms accounting for the invariable fixation of specific gravity at the level of about 1.010 are unknown.

Urinary specific gravities of 1.024 or higher may be observed in patients in whom the glomerular filtration rate has been significantly reduced. This dissociation of functions indicates the hazard involved in depending on a single test. When fixation of specific gravity at about 1.010 occurs in the terminal phase, it may persist for months or years and, thus, will not aid in evaluating further renal functional impairment in the course of the renal disease. In this same period, progressive decrease in the rate of glomerular filtration continues to serve as evidence of further functional impairment. In the rapidly accelerated phase of hypertensive disease, the normal concentrating capacity of the kidneys may be maintained to within a few weeks of death from uremia. This same phenomenon of dissociation between normal concentrating capacity and marked decrease in glomerular filtration with elevation of the blood urea concentration is observed in other rapidly progressive renal lesions, such as at the onset of acute diffuse glomerulonephritis. The reverse is frequently encountered for a period of months after clinical recovery from acute diffuse glomerulonephritis when complete loss of concentrating capacity may be associated with normal glomerular filtration rate and normal blood urea concentration.

In addition to its occasional undependability in rapidly progressive renal disease and after recovery from acute nephritis, the maximal concentrating capacity of the kidneys has limited value as a guide to the progressive renal impairment that characterizes the evolution of the hypertensive kidney. The first reason is that this capacity is unimpaired during the greater part of the course of hypertensive disease, despite the fact that loss of renal function can be demonstrated by reduction in the rate of glomerular filtration, effective renal blood flow, and maximal tubular excretory capacity. Secondly, its usefulness is limited by the fact that, when fixation of specific gravity has occurred, the maximal concentrating capacity can give no further information, while quantitative measurements of the discrete excretory functions demonstrate continuing renal functional impairment. These observations reemphasize the importance of multiple tests in evaluation of the multiple excretory functions of the kidneys.

The ability of the kidneys to form dilute urine with specific gravity of 1.001 to 1.004 is directly related to the rate of water excretion. In hypertensive disease, water excretion by the kidneys is unimpaired until late in the disease; the maximal concentrating power is decreased before the dilution is impaired. It is not uncommon for the maximal specific gravity to be reduced to about 1.010 at a time when the kidneys are still able to elaborate a dilute urine with a specific gravity of 1.001 to 1.004. Diluting capacity is finally lost and the specific gravity becomes fixed at 1.010.

It is probable that the loss of diluting power occurring in the terminal stage of hypertensive disease is related to marked decrease in the number of functioning nephrons. The complexity of those extrarenal factors, which affect the rate of the renal excretion of water, is such that the significance of variations in diluting power is difficult to interpret. Also, during recovery from acute diffuse glomerulonephritis, diluting power may return promptly to normal, while complete loss of concentrating power may persist for many subsequent months. The diluting power of the kidneys is, therefore, of little aid in the evaluation of the renal functional status.

PHENOLSULFONPHTHALEIN EXCRETORY CAPACITY

The capacity of the kidneys to excrete phenolsulfonphthalein (phenol red) is measured by determining the rate of excretion in a fixed period of time or the rate of its clearance from the blood. About 94% of injected phenolsulfonphthalein is removed from the blood by tubular excretion. Like iodopyracet and *p*-aminohippurate, although not to the same extent, a large percentage of the phenolsulfonphthalein is removed from the blood in one circulation through the kidneys. This clearance,

therefore, can be used to indicate relative variation in the effective renal blood flow. The normal value for phenolsulfonphthalein clearance is about 400 cc. per minute.

Phenolsulfonphthalein excretory capacity of the kidneys in renal disease is affected by specific impairment of the tubules that excrete dye and decrease in effective renal blood flow. The phenolsulfonphthalein clearance exhibits the same trend as the iodopyracet or *p*-aminohippurate clearance. The markedly decreased clearance observed during the terminal stages of renal disease represents the combined effect of decreased renal blood flow and the presence of numerous tubules that have lost their phenolsulfonphthalein excretory power.

The rate of excretion of dye in a fixed period of time is used more commonly as a measure of tubular excretion than is its clearance from the blood. Since the introduction of this test of renal function, the generally accepted method has been the estimation of the dye excreted in the urine in one and two hours after either intravenous or intramuscular injection. Determination of the percentage of phenolsulfonphthalein excreted in a fixed period of time is not as helpful as the estimation of its clearance from the blood because, by the accepted technique of measuring one and two hour urinary excretion, normal results may be obtained even when renal functional impairment exists. The probable explanation for this lack of sensitivity is related to the method used for the collection of phenolsulfonphthalein excreted in one and two hour periods. The intravenous or intramuscular administration of 6 mg. of dye does not raise or maintain plasma levels high enough to reach maximal tubular excretory capacity and, therefore, will not indicate early impairment of function. Actually, the administration of this amount of dye results in plasma levels at which a larger percentage of the dye is removed by the normal kidney in the first 15 to 20 minutes. When one and two hour collection periods are used, the kidneys, despite reduction in the renal blood flow or in their capacity to excrete the dye, are given the opportunity repeatedly to clear the blood of phenolsulfonphthalein. For this reason, a normal value for total two hour excretion may be obtained despite renal functional impairment, but it would differ from the normal in that the rate of excretion in the second hour would quantitatively approach the amount excreted in the first hour, whereas normal kidneys excrete the larger quantity in the first hour.

Form for Recording the Results of the Composite Kidney Function Tests

Name..... Age..... Sex..... Date.....

Diagnosis..... Weight..... Height..... Surface area.....

Specimen	1	2	3	4
Time	8 p.m.-8 a.m.	9:00 a.m.	10:00 a.m.	11:00 a.m.
Volume, cc.				
Maximal Concentrating Capacity Specific gravity			×	×
Glomerular Filtration Inulin clearance, cc. per minute	×	×		×
Renal Plasma Flow Para-aminohippuric acid clearance, cc. per minute	×	×		×
Maximal Tubular Excretory Capacity Para-aminohippuric acid Tm, mg. per minute	×	×	×	
Urinalysis				
Protein	×		×	×
Red blood cells	×		×	×
White blood cells	×		×	×
Casts	×		×	×
Blood urea, mg. per 100 cc.				
Remarks				

We have used the fractional method of dye excretion by utilizing three 20 minute urine collection periods. The urine is collected by urethral catheterization to insure complete emptying of the bladder, for in a 20 minute collection period incomplete bladder emptying can introduce a source of error. The average rate of excretion in 25 normal persons was 30% in the first 20 minutes and 55% in the first hour.[2]

When phenolsulfonphthalein is used to measure renal tubular excretion, the method of choice is the dye clearance. For routine clinical use, however, the excretion rate in a fixed period of time is adequate, and the fractional technique is preferable to hourly urine collection periods.

INFLUENCE OF SPONTANEOUS VARIATIONS IN URINE FLOW ON INTERPRETATION OF UNILATERAL RENAL FUNCTION

It has been observed that the rate of reabsorption of water by the tubules can vary at the same moment in the separate kidneys in normal persons and in patients with renal disease despite the fact that the kidneys have equal functional capacities. It is possible, therefore, to have different rates of urine flow at the same moment, and, as a result, the concentration of total solids or of specific substance can vary in the urines obtained simultaneously from the two equally efficient kidneys. Inequality in the urine flow from the two kidneys may lead to misinterpretation of comparative excretory tests of renal function. The concentration of urea, phenolsulfonphthalein, or indigo carmine may differ in the urine sample obtained simultaneously from two kidneys with equal function; variations are related to differences in urine flow rather than to unilateral functional impairment.

Differences in urine flow from the two kidneys can also account for significant variations in the appearance time of intravenously administered dye (phenolsulfonphthalein or indigo carmine). There is a large dead space in the collecting tubules, pelves and ureters, and, if the rate of urine flow is significantly lower in one kidney, the time necessary for urine-containing dye to traverse this dead space will be comparatively longer; the appearance time of the dye will vary inversely with the rate of urine flow.

PYELOGRAPHY

The ability of the kidneys to excrete water at different rates has particular significance when related to the interpretation of intravenous pyelography. Differences in the urinary concention of iodopyracet or any substance

2 Goldring, W., and Chasis, H.: Hypertension and Hypertensive Disease, New York, the Commonwealth Fund, 1944.

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used as a contrast medium may be referable solely to differences in the urine flow. This difference in concentration of the contrast medium will result in differences in intensities of roentgenologic shadows. Significant variations have been noted in the relative densities of pyelographic shadows in patients studied with kidneys of equal functional capacities. In these instances, a false conclusion might be drawn that the kidney excreting the more dilute urine and consequently producing the more poorly defined shadow was functionally inferior to the contralateral kidney, when, as a matter of fact, renal functional impairment when measured by the precise quantitative tests described was demonstrated to have progressed to the same extent in both kidneys.[2]

The rate of reabsorption of water by the tubules and hence the rate of urine flow may vary markedly in two kidneys of equal functional capacity. Excretory tests comparing the functions of the two kidneys should, therefore, be evaluated with caution for inequality in urine flow of itself can account for variations in urinary specific gravity, urea concentration, appearance time and relative concentration of dyes, and in the roentgen shadow in excretory pyelography.

COMPOSITE KIDNEY FUNCTION TEST

An ideal assessment of the various excretory functions of the kidneys can best be obtained from a composite test (see table). This complete assessment is especially valuable since, under some circumstances, the discrete functions of the kidneys may vary independently of each other. The composite test includes urinary specific gravity after a period of dehydration to measure reabsorptive capacity of the tubules, inulin clearance to indicate the rate of glomerular filtration, *p*-aminohippurate clearance to measure of effective renal blood flow, maximal rate of *p*-aminohippurate excretion to measure maximal tubular excretory capacity, the blood urea concentration, and chemical and microscopic examination of the urine. Preparation of the patient for this test as well as methodology have been described in detail elsewhere.[2]

In cases in which it is not feasible to apply the relatively difficult techniques suggested, comparable information may be obtained by omitting the measurement of maximal tubular excretory capacity and by substituting the urea clearance (or endogenous creatinine) for the inulin clearance and by substituting the fractional phenolsulfonphthalein excretion for the measurement of the effective renal blood flow.

SUMMARY AND CONCLUSIONS

The value and limitations of various kidney function tests are discussed. The ideal measurements involve quantitative estimates of the rate of glomerular filtration, effective renal blood flow, and maximal tubular excretory capacity. For this purpose a composite test is suggested. This composite test may be simplified for clinical use if the more involved techniques are not feasible. This simplification utilizes the maximal urinary specific gravity after a period of dehydration as a measure of tubular reabsorptive capacity, the urea clearance (or endogenous creatinine clearance) and blood urea concentration as an approximation of the rate of glomerular filtration, and the fractional excretion of phenolsulfonphthalein as a measure of tubular excretory capacity.

In view of the multiplicity of renal excretory functions and the fact that in renal disease these may vary independently in each kidney, it is evident that no single test is adequate for complete assessment of the over-all functional capacity of the kidneys.

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SURGICAL MANAGEMENT OF ULCERATIVE COLITIS

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and
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Noteworthy progress in the therapeutic approach to chronic ulcerative colitis is rapidly being achieved in the field of surgery. The general practitioner, internist, gastroenterologist, and psychiatrist alike are viewing surgical intervention with increasing assurance, and less and less frequently are seriously ill patients reaching the operating table too late for curative treatment. This fact is self-evident when one examines the remarkable fall in surgical mortalities in ulcerative colitis during the past decade as compared with previous decades. A no less significant observation is the fall in the incidence of emergency ileostomies. By virtue of awakened interest and cooperation between all fields of therapy, surgical measures are well planned and it is common to see the successful completion of total colectomy with cure of the disease brought about in two operative stages or less.

In our series of 331 patients with chronic ulcerative colitis, 81, or 24.5%, have undergone surgical intervention. The post operative mortality is 5, or 3.4%, in 137 operations performed. Four of the mortalities were the result of emergency ileostomies undertaken in almost moribund patients prior to 1946. Of particular interest is the fact that in the last five years it has been necessary to perform emergency loop ileostomies in only two patients. The remaining patients of our surgical group in this period have reached us in time for intensive whole blood transfusions, and antibiotic and electrolyte administration prior to operation. Preoperative preparation has been managed with the cooperation of an internist in all cases and often with the supplemental opinions of a gastroenterologist and a psychiatrist. With this coordinated plan of action it has been possible to perform ileostomy and colectomy in one stage in a majority of

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patients. There have been no postoperative mortalities in this group, and convalescence has been significantly shortened.

SURGICAL INTERVENTION IN CHRONIC ULCERATIVE COLITIS

All of us are aware of the lifesaving role surgery plays in the patient with intractable ulcerative colitis who is acutely ill and in a toxic state. The indication for surgery in these persons is at once apparent when other remedies fail. It is not this phase of the disease, however, that we are concerned with here, it is rather the so-called borderline patient who experiences remissions and exacerbations and, while at times is very ill, at other times seems to be able to carry on with his occupation. This is the commoner form of chronic ulcerative colitis, and in such persons we do not find the classical indications for operation such as perforation (or impending perforation), hemorrhage, obstruction, abscesses, fistulas, progressive toxemia, and severe nutritional and electrolyte deficiencies. In this chronically ill patient we must carefully balance the advantages to be gained by surgery against the risk of operation and the almost certain institution of a permanent ileostomy.

The greatest single benefit to be achieved by colectomy is the cure of the disease. To the patient this means freedom from episodes of incapacitating diarrhea or dysentery, the termination of arthritic symptoms, a cure of chronic annoying anorectal disorders such as recurring fissures, fistulas, stenosis, proctitis, and others, a curbing of thromboembolic phenomena, a cessation in progressive degenerative liver and kidney changes, and the prevention of primary cancer in the rectum and colon by the removal of a precancerous bowel.

CARCINOMA FOLLOWING CHRONIC ULCERATIVE COLITIS

Despite a preponderance of evidence to the contrary, there are still wishful thinkers who would attribute the incidence of carcinoma in chronic ulcerative colitis to other conditions. Otani and Snapper [1] would lead us to believe that (1) multiple familial polyposis accompanying ulcerative colitis is an underlying etiological factor, (2) adenomatous polyps coexistent with chronic ulcerative colitis undergo malignant changes, or (3) ulcerative colitis is secondary to a stenosing malignant lesion. Our own experience has not supported these assumptions. Each of the possibilities named present distinct characteristics not to be confused with carcinoma arising from chronic ulcerative colitis. In our series of 45 colectomies there were five patients who had large bowel carcinomas, an incidence of 11.1%. In four patients the lesions were unsuspected preoperatively. In no patient were there coexistent adenomatous polyps, familial histories of cancer of polyposis, or diagnoses of chronic ulcerative colitis that did not antedate the discovery of cancer by considerable lapses of time. In only one patient was the history of ulcerative colitis less than five years in duration. In three patients the disease had been present over a period of 15 years or more. In each extirpated colon and rectum the carcinomatous lesions resembled one another and were not characteristic of the usual carcinomas seen arising from adenomatous polyps. Invasion of the submucosa and muscularis was extensive, and the lesions were of a highly undifferentiated type. In two patients metastasis was widespread. For comparison, a patient with familial polyposis (not included in this series) with ulcerative colitis of two years' duration was selected. In this patient's excised colon, ulceration was widespread, with destruction of mucous membrane, but the adenomatous polyps were distinct, easily identified, and histologically differentiated from inflammatory polyps. Three carcinomas were present, and numerous polyps presented atypical changes.

Counsell and Dukes [2] found an incidence of 11.1% carcinoma in a series of 63 patients undergoing surgery for ulcerative colitis. They conclude that chronic ulcerative colitis predisposes to carcinoma, and they feel that the extent of this predisposition has been underestimated because of inadequate follow-up of patients with ulcerative colitis and because of clinical difficulties in diagnosis. They point out that carcinoma following chronic ulcerative colitis usually grows rapidly and metastasizes early. "It may cause no recognizable surface tumor or ulcer but only a diffuse stricture resulting from intramural spread of cancer." Shands, Dockerty, and Bargen [3] describe the striking evidence of multicentricity in 19 of 40 patients with adenocarcinoma occurring in chronic ulcerative colitis. This suggests that the origin of these secondary adenocarcinomas is in scattered foci within the mucosa.

When cancer occurs in patients with chronic ulcerative colitis, it characteristically develops in late adolescence or early adulthood, and exacerbations are experienced intermittently for periods of 10 years or more. Four of our five patients fit into this category. In each, cancer resulted before the age of 50 years. Kiefer and his associates [4] write, "A person who acquires ulcerative colitis in the second decade of life and continues to suffer from active disease until he is 30 faces a real hazard in possible malignant degeneration." Lyons and Garlock,[5] in their series of surgical patients having the disease for over 12 years, report a 36% incidence of carcinoma. Of 16 patients with ulcerative colitis involving the rectum for over 12 years, in 7, or 43%, carcinoma developed.

Pseudopolyposis is not an uncommon occurrence in advanced ulcerative colitis. In our practice we consider it an indication for colectomy. Our reasoning is based on the finding of literally hundreds of inflammatory polyps in each of the colons of the five patients in our surgical group who were discovered to have rectal or colonic cancers complicating their disease. Shands, Dockerty, and Bargen [3] report 19 cases of pseudopolyposis in a series of 40 specimens of ulcerated large bowel wherein carcinomatous change had taken place. In their series, however, histopathological evidence of multicentricity of the adenocarcinomas was present in 21 specimens, and of these, 16, or 76.2%, were accompanied by pseudo-

1. Otani, S., and Snapper, I.: On the Incidence of Carcinoma in Chronic Ulcerative Colitis, J. Mt. Sinai Hosp. **19**: 275, 1952.
2. Counsell, P. B., and Dukes, C. E.: The Association of Chronic Ulcerative Colitis and Carcinoma of the Rectum and Colon, Brit. J. Surg. **39**: 485, 1952.
3. Shands, W. C.; Dockerty, M. B., and Bargen, J. A.: Adenocarcinoma of the Large Intestine Associated with Chronic Ulcerative Colitis, Clinical and Pathologic Features of 73 Cases, Surg., Gynec. & Obst. **94**: 302, 1952.
4. Kiefer, E. D.; Eytinge, E. J., and Johnson, A. C.: Malignant Degeneration in Chronic Ulcerative Colitis, Gastroenterology **19**: 51, 1951.
5. Lyons, A. S., and Garlock, J. H.: The Relationship of Chronic Ulcerative Colitis to Carcinoma, Gastroenterology **18**:170, 1951.

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polyposis. The development of inflammatory polyps is a late manifestation that usually takes place after the disorder has been present for six years [6] or more. It is typically found in the healing bowel that is undergoing remission,[7] and this process of healing and remission, with later exacerbation and repetition of the cycle, is the usual history of events in those patients in whom cancer develops. Inflammatory polyps may disappear in many of these patients with long periods of remission,[8] and without doubt it is in these persons that considerable danger exists, especially when the disease has been present for 10 years or more.

It would then seem imperative that patients who have had recurring exacerbations of chronic ulcerative colitis over a long period of time be considered fit subjects for colectomy and excision of the rectum. Indeed, in such persons, even if the hazard of malignant degeneration is not considered, surgical management is mandatory if a cure of the disease and escape from crippling secondary organic changes is to be insured.

CHOICE OF PROCEDURE

In our approach to the selection of an operation for ulcerative colitis we believe that ileostomy alone, as a definitive or curative measure, has no place in the surgeon's armamentarium. Further, we do not recommend ileostomy for any patient unless there is indication that the ileostomy should be accompanied by colectomy or that colectomy should be performed at a later stage. We find one-stage ileostomy combined with colectomy a most acceptable and useful technique.[9] Patients with acute exacerbations or progressive fulminating disease respond dramatically. In contrast to ileostomy alone, we observe that postoperative disability is especially lessened by a more rapid adjustment of the ileum to the functions of the colon in the absence of the colon. There is less toxicity, as evidenced by lowered temperatures and pulse rates. Nutrition, fluid, and electrolyte balance are more quickly restored, and the patient is not faced with greater surgery to follow.

We do not attempt preservation of the rectum with the thought of utilizing it in the future. Despite interruption of the fecal stream by ileostomy, there is a danger of carcinomatous change. Furthermore, it has been evident that, even with the lapse of several years, complete rectal healing is unlikely. Drainage is generally continuous, and there is practically no hope that a once diseased rectum can ever be restored to satisfactory function. Transplantation of the ileum to the anus in an attempt to reconstruct the continuity of the bowel has not been generally accepted. Postoperative complications and difficulties in rehabilitation are greatly increased, and we have not felt justified in subjecting patients to this further surgery.

We have long ceased to feel apologetic or reluctant in recommending permanent ileostomy. The patient and his family are clearly advised, without reservation, concerning the nature of an ileostomy and the care that it will require. That this approach is justified is aptly shown by the average patient, who unhesitatingly learns to care for himself and quickly progresses to complete rehabilitation. Most of these patients are able to assume responsibilities that were unthinkable in their previous physical state.

ACHIEVEMENTS IN SURGERY OF CHRONIC ULCERATIVE COLITIS

Ileostomy.—In the past, most of the complications following operative intervention for chronic ulcerative colitis centered about the ileostomy. Little was known of the nature of electrolyte, nutritional, and fluid losses from this artificial opening. Replacements were often inadequate, with the result that patients were greatly retarded in their convalescence. Today this difficulty has been largely overcome. We are now much more conscious of the importance of fluid, potassium, and sodium deficits. Accurate techniques are available for measuring the circulating blood volume, and we are no longer at a complete loss in estimating nitrogen deficiency. We have newer and better means of supplying calories and proteins, and we are more than ever aware of the great part that whole blood restoration plays in the postoperative course. Newer electrolyte solutions are available for intravenous use. Fewer difficulties related to electrolyte, fluid, and nutritional losses have been noted in the newer simultaneous ileostomy and colectomy procedure because of an earlier adaptation of the ileum to the absorption of these materials.

In the past, ileostomy was often the source of partial or complete intestinal obstruction. This complication could, in almost every case, be traced to haphazard and faulty technique arising from haste and inattention to the fine details of ileostomy construction. Preventable partial obstruction of the stoma due to narrowing of the stab wound or skin incision was overlooked, and usually little or no attention was given to utilizing the cut edge of the free mesentery to anchor the distal ileum. By suturing of this free border to the anterior abdominal wall, torsion or the wrapping of intestine around the illeum was found to be prevented, and prolapse of the stomas was no longer a possibility. The combination of ileostomy with colectomy [10] brought with it the discovery that postoperative adhesions could be considerably lessened by the removal of the diseased colon.

Intermittent or partial obstruction of the ileostomy noted in some of our early patients was often complicated by the development of ulcerative changes in the ileum. Two of these patients required resections of several feet of the terminal small intestine. These experiences with ulcerative ileal recurrences caused by partial obstruction parallel those of McKittrick and Miller [11] and Dennis and Karlson.[12] The care of the skin is of minor concern because of the arrival on the market of simple skintight, lightweight appliances. Attention must be directed to-

6. Coffey, R. J., and Bargen, J. A.: Intestinal Polyps: Pathogenesis and Relation to Malignancy, Surg., Gynec. & Obst. **69**:136, 1939.

7. Bargen, J. A., and Comfort, M. W.: The Association of Chronic Ulcerative Colitis and Multiple Polyps, Ann. Int. Med. **4**:122, 1930.

8. Swinton, N. W., and Warren, S.: Polyps of the Colon and Rectum and Their Relation to Malignancy, J. A. M. A. **113**:1927 (Nov. 25) 1939.

9. Footnotes 1-13. Trimpi, H. D., and Bacon, H. E.: The Evolution of Surgical Supervision in the Management of Advanced Idiopathic Ulcerative Colitis, Rev. Gastroenterol. **18**: 325, 1951.

10. Bacon, H. E., and Trimpi, H. D.: The Selection of an Operative Procedure for Patients with Medically Intractable Ulcerative Colitis, Surg., Gynec. & Obst. **91**:409, 1950.

11. McKittrick, L. S., and Miller, R. H.: Idiopathic Ulcerative Colitis: A Review of 149 Cases, with Particular Reference to the Value of, and Indications for Surgical Treatment, Ann. Surg. **102**: 656, 1935.

12. Dennis, C., and Karlson, K. E.: Surgical Measures as Supplements to the Management of Idiopathic Ulcerative Colitis: Cancer, Cirrhosis, and Arthritis as Frequent Complications, Surgery **32**: 892, 1952.

ward the placing of the ileostomy to allow for fitting of a correct bag, but if this has been done correctly there need be no leakage of intestinal contents. The Koenig-Rutzen, Jonas, Pierce, and Perry appliances have all been very satisfactory in our hands.

Colectomy.—There is very little doubt today in the mind of any surgeon dealing with chronic ulcerative colitis that a one-stage colectomy is superior to the frequent stages that characterized the operation in the past. A signal advance was attained when the three stage operation, ileostomy followed by colectomy, followed by excision of the rectum, with suitable time intervals between each, replaced the older five-stage or six-stage procedure. In the last few years we have found further progress in the employment of two stages, the first for ileostomy and colectomy, and the second for extirpation of the rectum. Recently we have satisfactorily performed the one stage operation (ileostomy and total colectomy with perineal proctectomy) in seven patients without mortality or increased morbidity.

The technical difficulties of colectomy are few. Considerable judgment is necessary, however, in determining at what point to divide the terminal ileum. If too much small bowel is sacrificed, there are increased postoperative losses of fluids and electrolytes. If too little is removed, the hazard of leaving diseased terminal ileum in situ is a reality. Frozen section has been suggested as being superior to gross study of the bowel to determine the extent of inflammatory involvement, and we would recommend every aid available in making this decision.

A problem arises regarding the site of amputation of the distal large bowel. Experience has taught us to avoid attempts to close any segments of ulcerated intestine leaving them within the abdomen or in retroperitoneal positions. Therefore, we elect to divide the low sigmoid and let the distal segment remain in the lower pole of the wound rather than to amputate the diseased rectum and close the distal segment. Abscess and sepsis are likely to occur. After the occurrence of perirectal infection in two of our patients, we concur with Miller, Gardner, and Ripstein [13] that the conservative measure is best adhered to. An alternative is, of course, to extirpate the rectum at the same time.

Abdominoperineal Excision of the Rectum.—We have had little or no problem in the abdominal approach to mobilizing the distal sigmoidal and rectal segment and removing it via the perineum by means of a modified Miles procedure some weeks after colectomy. In the male, care must be taken not to injure the vas or seminal vesicles, and in both sexes the levators and other perirectal structures are disturbed as little as possible so that bladder and sexual dysfunctions are avoided.

A question arises concerning the advisability of leaving the rectum for future anastomosis. Our experience with this maneuver has been discouraging, and a review of the literature would seem to support our findings. The outstanding complication is a recurrence of the disease in a supposedly healed rectum, even though a year or more is allowed to elapse before the ileum is brought down to anastomose. We performed the procedure in three patients. In two, it was later necessary to reestablish the ileostomy and excise the rectum. In all three cases the rectal manifestations of colitis were mild, and complete healing occurred before anastomosis. Danger of carcinomatous change in the preserved rectum cannot be overlooked because it is well known that cancer will develop even in the absence of the fecal stream, and in ulcerative colitis the rectum is the commonest site for its development.

13. Miller, G. G.; Gardner, C. M., and Ripstein, C. B.: Primary Resection of the Colon in Ulcerative Colitis, Canad. M. A. J. **60**: 584, 1949.

SURGICAL RESULTS

Of 331 patients with chronic ulcerative colitis who were studied and treated by us, 81, or 24.5%, were operated on. Ileostomy alone was performed in 36 patients, with a mortality of 4, or 11.1%. Colectomy and abdominoperineal excision of the rectum were performed in 45 patients without a single postoperative fatality. Among the 81 patients undergoing surgical treatment a total of 145 operations were performed. Ileosigmoidostomy with colectomy was achieved in three patients, but in two of these it was later necessary to establish permanent ileostomies and excise the rectum. Twenty-eight miscellaneous operations were carried out, consisting primarily of ileostomy revisions. Four patients underwent lysis of adhesions, two had drainage of abdominal abscesses, and in two it was necessary to resect the distal ileum. One of these latter patients died postoperatively. Wound disruption was noted in one patient, but repair was followed by complete recovery. Five patients had carcinoma, and two of these died of carcinomatosis within two years after operation. In the remaining three, who are alive and well, sufficient time has not elapsed to record proper survival evaluations. Of 45 total colectomies and 42 excisions of the rectum, complete rehabilitation has been attained in 41 cases, a rehabilitation rate of 91.1%. Two rehabilitated housewives of the colectomy group became pregnant and successfully carried to term viable infants. In both instances labor and delivery were normal.

SUMMARY

Great achievements have highlighted the progress of surgical management in chronic ulcerative colitis during the past decade. The cooperation of all fields of therapy has been outstanding in bringing the patient who is intractably ill to surgery before irreversible and fatal secondary functional and organic changes have supervened. Of a series of 331 patients with chronic ulcerative colitis treated by us since 1940, 81, or 24.5%, underwent surgical intervention. A total of 145 operations were performed, with a surgical mortality of 5, or 3.4%. Four of these deaths occurred prior to 1946, as the result of emergency ileostomies in practically moribund patients.

Particular attention is directed to the patient with a longstanding chronic illness who experiences exacerbations and remissions every few months or years, and who is never ill enough at any one time to indicate immediate surgical intervention, but who eventually is either totally disabled or succumbs to secondary organic complications. Colectomy must be considered. Weighed against the low surgical risk and the inconvenience of a permanent ileostomy are the benefits of cure of the disease, removal of a precancerous bowel, and prevention of

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thromboembolic disease and a reversal of degenerative liver, kidney, and arthritic changes.

Five cases of cancer complicating chronic ulcerative colitis are reported. These adenocarcinomas were discovered in specimens of colon and rectum from a series of 45 colectomies in which complete colectomy was performed (incidence of 11.1%). In four cases, cancer was not suspected preoperatively. In each specimen the lesions were diffuse, invasive, and of high grade, and there were numerous accompanying inflammatory polyps. We recommend for the surgical management of ulcerative colitis, a two-stage operation, the first stage to consist of ileostomy and colectomy down to the low sigmoid colon and the second stage to be an abdominoperineal excision of the rectum and distal sigmoid. Ileostomy carefully performed concomitantly with the extirpation of the diseased colon affords the patient less difficulty in adjustment than ileostomy alone. Modern appliances and receptacles are lightweight and are easily worn without discomfort or annoyance. The patient is permitted to return to full employment, often to occupations prohibited to him prior to operation because of ill health. Ileostomy, unless it be followed or accompanied by colectomy, is not recommended. Excision of the rectum and distal sigmoid colon must be performed in each patient undergoing colectomy. Of 45 patients undergoing colectomy with excision of the rectum, 41 have been completely rehabilitated (a rehabilitation rate of 91.1%). In the rehabilitation group are two mothers who have recently become pregnant and successfully carried to term viable infants with normal labors and deliveries.

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RATIONAL USE OF ANTIBIOTICS IN CONTROL OF SURGICAL INFECTIONS

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It is a truism to say that the antibiotics have altered the natural course of pathological conditions that have been designated surgical infections. These infections are pathological processes produced in the human or animal body by the entrance of bacteria into the tissues causing either an exudation of leukocytes into a localized area of necrosis or an exudation of leukocytes into a body cavity without necrosis but with the formation of a fibrinous clot. Such pathological processes formerly required a surgical procedure for their control, either excision of part or all of the area of inflammation or incision for removal of the exudate, necrotic tissue, and bacteria that they contain.

The antibiotics have been distributed widely throughout the world, and in places in which they are generally available it is now the responsibility of the surgeon to use them to the best of his knowledge and ability, to prevent bacteria from gaining a foothold in the body when they have entered through the operative wound or at the time of an accidental wound or burn, and to stop their activity as abruptly as possible, if he finds that the bacteria have already become established in the tissues when the patient comes for help. To aid him in those purposes, the surgeon now has available not only his scalpel but eight or nine antibiotics and several other chemotherapeutic agents. Inasmuch as a surgical procedure of itself will often bring the progress of a surgical infection to a standstill, it is at times difficult to be sure that the use of the antibacterial agents in addition or as an adjunct to surgery will achieve these purposes any better than surgery alone. Some time ago one of us (F. L. M.) suggested five criteria by which one could judge that the antibiotics are of some use in surgical infections. These criteria are met when (*a*) the antibiotics obviate the necessity for surgery entirely, (*b*) they permit a less extensive surgical procedure, (*c*) they actually shorten the healing and recovery time, (*d*) they permit a successful primary closure after removal of the focus of infection, which otherwise would not be possible, and (*e*) they permit an earlier secondary closure than would otherwise be done. Further confirmation of the effectiveness of the antibiotics is demonstrated when the purulent exudate suddenly ceases or the wound cultures become negative.[1]

The knowledge of how best to use the antibiotics and which ones to use in any given case is imperative. If penicillin were a panacea or the only antibiotic available, the decision would be easy, but the very multiplicity of antibacterial agents, each with its respective advantages and disadvantages, makes the wise choice difficult. Undoubtedly more antibiotics will be discovered and will complicate the picture still further. It is our hope that this paper will transmit some of our experience in this field.

It requires continuous vigilance, but the rewards are gratifying when infections respond to specific therapy. This vigilance is essential because every accident and every surgical procedure has the potentialities of infection and at least one-third of the cases on a general surgical service are problems of infections well established before admission to the hospital.

It is our purpose to outline a program of procedure so that more patients will have the fullest benefit of our knowledge of the antibiotics. It is also our aim to restore the patient as soon as possible to normal form and function and thus shorten disability, minimize economic exhaustion, and prevent physical disfigurement or death.

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1. Meleney, F. L.: Difficulty of Evaluating Drug Treatment in Surgical Infections, J. A. M. A. **124**: 1021-1026 (April 8) 1944.

What are the conditions met by a surgeon that offer the opportunity for employing antibiotics intelligently? These may be classified in two groups—those responding to either prophylactic or active measures.

PROPHYLACTIC USE OF ANTIBIOTICS

Clean Wounds.—The surgeon is interested first of all in preventing infection in operative wounds. All of the minutiae of sterile technique have been developed with that end in mind—the autoclaving of dry goods and solutions, the boiling of instruments, the scrubbing of hands of the operating team, the masking of noses and mouths, the preparation of the operative field, the avoidance of air contamination, the use of silk and cotton for suture material, the gentle handling of tissues, and careful hemostasis. All of these procedures should bring the incidence of wound infection in a clean field to less than 2% and in serious infections to less than 1% in any well-run operating room.

What place have antibiotics in the prophylaxis of infection in clean wounds? Should 50 patients receive an antibiotic or a combination of antibiotics to prevent infection in one of them? No! It is our belief that antibiotics should not be used with clean fields except for certain categories that will be mentioned below. To use antibiotics in clean operations is an admission that the sterile technique in the operating room is not up to the requirements, and it is likely to drop to still lower levels if breaks in technique are not corrected because the surgeon will say, "Oh, never mind. An antibiotic will take care of that."

There are, however, certain cases in which, if infection occurs, it is a very serious matter. These are operations on the brain and on the heart. These are often long procedures, and, therefore, the chance of air contamination is increased. In a somewhat lower category, from the point of view of the frequency of infection, are the long plastic procedures on the neck, chest, and breast.

What antibiotics should be used in these cases, and how should they be used? The condition with which the surgeon has to deal is a wound with relatively few organisms on freshly cut surfaces. The ideal treatment is a fine spray of 5 to 10 cc. of the antibiotic into all crannies of the wound during closure. Thus direct contact with contaminating organisms can be obtained. Furthermore, the best antibiotic is one that is bactericidal. By using such an antibiotic the organisms can be killed directly and are given no chance to gain a foothold. They are not merely held in check as they would be by a bacteriostatic agent requiring the bacteria to be destroyed by the body defenses.

TABLE 1.—*Resistance to Penicillin of Coagulase-Positive Micrococcus (Staphylococcus) Aureus**

Year	No. of Strains	% Resistant
1947-1948	286	17.8
1949	228	29.1
1950	269	43.5
1951	293	43.0
1952	290	31.1
1953 (Jan. 1-May 1)	269	22.3

* Recovered from infections treated in outpatient department, Surgical Service, Presbyterian Hospital, New York.

The commonest contaminating organisms in clean operations are the micrococci (staphylococci) from the air and from the skin of the patient. If the operating team personnel does not adequately mask the nose as well as the mouth, another abundant source of micrococci is open to the sterile field. The most reasonable antibiotics to choose are penicillin, bacitracin, streptomycin, or neomycin (table 2). All of these are bactericidal and potent against micrococci. Penicillin or bacitracin, in a concentration of 1,000 units per cubic centimeter, may be sprayed on the operative field and are preferable to streptomycin and neomycin. In recent years, however, with a large percentage of micrococci resistant to penicillin and with patients becoming increasingly sensitive to penicillin, bacitracin is taking on a more important role. Patients are seldom allergic to bacitracin. On brain surfaces, bacitracin is much less toxic than penicillin, and this fact makes it preferable as a prophylactic in neurosurgical procedures. For effective local use, streptomycin requires a concentration of 0.5% and neomycin 1%. On large fresh wounds, which are to be closed, neomycin might prove to have a systemic toxic effect.

TABLE 2.—*Resistance of Coagulase-Positive Micrococcus (Staphylococcus) Aureus** to Various Antibiotics*

Antibiotic	% Resistant
Penicillin	22.3
Bacitracin	7.1
Streptomycin	10.0
Oxytetracycline (Terramycin)	15.5
Neomycin	1.0

* Recovered from infections treated in outpatient department, Surgical Service, Presbyterian Hospital, New York, Jan. 1-May 1, 1953.

During the last few years, reports have come from many sources that micrococci have become increasingly resistant to penicillin. Some reports go as high as 60 to 80%.[2] Our own experience showed this trend during the first two years of the extensive use of penicillin, but in 1951 the rise in the percentage of resistant strains came to a standstill in infections treated in outpatients. In the past two years it has fallen again (table 1). We believe we were the first to call attention to this fact and have put forward the theory that the phenomenon may be due to the widespread use of bacitracin and the combination of chlortetracycline (aureomycin), oxytetracycline (Terramycin) and chloramphenicol (Chloromycetin).[3]

Table 2 shows our most recent experience with tests for sensitivity and resistance of micrococci to the five antibiotics that we use oftenest and against which we routinely test every culture that comes to the laboratory. Table 3 gives a comparison of the action of bacitracin and neomycin against the major strains of organisms coming to the Surgical Bacteriological Laboratory from all surgical services except otolaryngology and dermatology. This shows how bacitracin and neomycin complement one another for local therapeutic effect.

Antibiotics given systemically are not usually indicated in clean fields for, if potent bactericidal antibiotics are

2. Barber, M., and Rozwadowska-Dowzenko, M.: Infection by Penicillin-Resistant Staphylococci, Lancet **2**: 641-644 (Oct. 23) 1948. Dukes, C. D.: Importance of Specific Antibiotic Therapy in Surgical Infections, Am. Surgeon **18**: 778-783 (Aug.) 1952.

3. Meleney, F. L., and Johnson, B. J.: Clinical Significance of Increasing Resistance of Organisms for the Antibiotics, Surg., Gynec. & Obst. **97**: 267-276 (Sept.) 1953.

applied to the surface of the fresh wound, any casual contaminating organisms are not given the opportunity to multiply and invade the deeper tissues. When administered systemically, the antibiotic reaches the wound area in very dilute form. If infection develops in spite of the local prophylactic antibiotic, because the contaminating organisms are resistant to the antibiotic used, cultures will determine the nature of the infection and the sensitivities of the causative organisms to some other available antibiotic, which should then be employed.

Contaminated Fields.—There is, however, a real indication for the use of antibiotics prophylactically in contaminated fields of operation. Bacteria on mucous membrane surfaces of the body cannot be destroyed or reduced in number as readily as they can be on the skin. Operations that expose the tissues to contamination from these sources have, therefore, a greater chance of becoming infected. The incidence of infection in these fields may be 20 to 25% in a well-ordered operating room, if antibiotics are not used. It is reasonable to give antibiotics to four or five patients to prevent infection in one. This applies to operations on the eye, ear, nose, throat, mouth, esophagus, stomach, duodenum, jejunum, ileum, colon, vagina, and penis.

TABLE 3.—*Results of Tests for Sensitivity to Neomycin and Bacitracin*

Species *	No. of Strains	% Sensitive to	
		Neomycin	Bacitracin
Coagulase-positive Micrococcus (Staphylococcus)	397	99.0	89.0
Coagulase-negative Micrococcus (Staphylococcus)	98	100.0	89.5
Hemolytic Streptococcus	100	58.0	85.0
Nonhemolytic Streptococcus	241	34.4	89.2
Coliform group	200	97.5	....
Proteus group	135	91.0	....
Pseudomonas group	49	34.7	....
Clostridium welchii	29	10.3	100.0

* Recovered from infections treated on all surgical services, Presbyterian Hospital, New York, Jan. 1-May 1, 1953.

It must be remembered that the contaminating organisms are different in different parts of the alimentary tract. The organisms most commonly found must constantly be kept in mind, and the appropriate antibiotic or mixture of antibiotics must be used. In fact, in elective procedures, it is best to take cultures from the operative field a few days before operation and to test the sensitivities of the organisms found.

The organisms that commonly contaminate operative wounds made on the nose are micrococci and nonhemolytic streptococci. On the mouth and esophagus they are the nonhemolytic and anaerobic streptococci, and, where there is a chronic pyorrhea, spirochetes and fusiform bacilli. The stomach with normally acid gastric juice often yields sterile cultures because of the acidity of that secretion. When organisms are found in the stomach or duodenum, they are usually the nonhemolytic streptococci, which are able to persist longer than other organisms in the acid environment and often pass into the duodenum. These species are also present in the jejunum, and here the gram-negative rods of the coli group begin to appear and a little further down, the clostridia, including the Welch bacilli. These three groups increase in number and variety from above downward; they are in greatest concentration in the lower ileum. When they pass the ileocecal valve into the colon, they begin to die in great numbers, so that when the stool is passed out of the rectum, although one-third of the mass is made up of bacterial bodies, most of them are dead.

Operations on the stomach and intestine have been carried out for many years through a clean abdominal wall. The operative field is only contaminated when the bowel is entered. Contamination can be minimized by various closed methods of anastomosis, but with the open methods now widely used, contamination varies greatly according to the care taken to prepare the bowel either mechanically or chemically beforehand and the care taken to prevent spillage. In recent years more and more procedures on the alimentary tract are carried out through thoracic or thoracoabdominal incisions, thus exposing the mediastinum and the pleural cavities to contamination. Often leaks from esophageal or esophagogastric anastomoses, duodenal stumps, gastroenterostomies, or enteroenterostomies are attributed to faulty suturing, but it is our contention that contaminating bacteria are oftener responsible for the failure of these anastomoses to heal and this results in leakage. Such leaks are more apt to occur when the anastomosis is above the stomach than when it is below, because the contamination above is from the mixture of mouth organisms that may be particularly numerous and synergistic, especially if mouth hygiene is bad. The next commonest site of leakage is in the lower ileum, because the intestinal organisms there are most numerous and viable.

It is, therefore, the responsibility of the surgeon to use every means available to minimize the contamination of the operative field whenever he is working along the alimentary tract. Mouth organisms may be reduced by dental care preliminary to any operation on the throat or esophagus, but this is not enough because the bacteria can be further reduced or discouraged by the local use of antibiotics. Bacitracin is particularly useful in this region because it is potent against the nonhemolytic streptococci, the anaerobic streptococci, and the spirochetes of the mouth, and it seldom if ever causes any allergic reaction in the mouth. Bacitracin requires the addition of an antibiotic potent against the gram-negative rods for action further along the alimentary tract, and here neomycin seems to serve well. Neomycin is weak against the streptococci and clostridia, but it is potent against most strains of Esch. coli and particularly of Proteus, which is resistant to almost all of the other antibiotics (table 3).

Both bacitracin and neomycin are bactericidal and are compatible with each other. We have demonstrated their synergistic action many times but never antagonism. Tablets are commercially available containing 2,500 units of bacitracin and 25 mg. of neomycin. These may be dissolved slowly in the mouth once every four or six hours to get the maximum effect in the mouth and esophagus or in the stomach. If the effect is desired in the lower intestine, four tablets should be swallowed every four or six hours. As neither of these antibiotics is absorbed, they continue their maximum action all along the alimentary tract. There is no need for fear of any systemic toxic reactions. Often when cultures are taken from the

esophagus and stomach and at the site of bowel resection sterile cultures are obtained after the administration of bacitracin and neomycin, as described above, for 48 or 72 hours. We have not seen or heard of either staphylococcic or proteus enteritis following their use in this manner.

Chlortetracycline, oxytetracycline, and chloramphenicol have all been used, and favorable results have been reported. These three antibiotics, however, are often not well tolerated in the mouth and, therefore, are not available for action on mouth organisms. All of them are partially absorbed from the intestine, and the amount available to inhibit the multiplication of organisms in the large intestine is uncertain. Furthermore, they frequently cause gastrointestinal upsets, with nausea and diarrhea, and often make it necessary to discontinue treatment. Oxytetracycline seems to be the least objectionable in these respects, and, if diarrhea does occur, it can generally be controlled. The association of chloramphenicol with aplastic anemia must be kept in mind. It does not seem advisable to us to run the risk of using it when other measures are superior. Monilial superinfections occur in some cases treated with chlortetracycline, oxytetracycline, or chloramphenicol, and the Proteus bacilli and Micrococcus aureus may multiply prodigiously in the bowel. For these reasons we do not consider any of these three so-called broad spectrum antibiotics optimal for this purpose.

Phthalylsulfacetimide (Thalamyd) has been found to be the most effective of the sulfonamides in reducing the number of intestinal organisms, but the preparation of the bowel with it usually requires five or six days, while the combination of bacitracin and neomycin will often give a sterile culture at the operative site in 48 hours. Further studies are necessary to determine whether it is advisable and more effective to combine phthalylsulfacetimide treatment with antibiotics.

Polymyxin B and chlortetracycline have been combined independently with bacitracin with favorable results, but neither polymyxin B nor chlortetracycline has as wide a spectrum over the gram-negative rods as neomycin, which is effective against most strains of the proteus group. Neomycin has been used alone with good reports of its effectiveness, but its weakness against the clostridia and the intestinal streptococci, both hemolytic and nonhemolytic, leaves a gap in the coverage of the intestinal organisms; this gap is closed by bacitracin. Of 29 strains of Clostridium welchii recently tested, all were susceptible to bacitracin but only 10% to neomycin (table 3).

At the time of operation, the surgeon should take a culture from the lumen of the alimentary tract at the site of operation, wherever that may be, so that he will know within 24 hours what organisms, if any, have contaminated the operative field. If any organisms are still viable in the lumen of the gut, the surface of the tissues at the level of operation will be contaminated by these residual bacteria. It is rational to assume that in every case some of the intestinal organisms have contaminated the operative site. In the past, it has been considered adequate in our hospital to apply a mixture of 20 mg. of streptomycin and 5% *p*-aminomethylbenzene sulfonamide (Sulfamylon) in 100 cc. of water to the area of operation within the abdominal cavity, as advocated by Howes.[4] Recently we have advised the addition to this of 20,000 units of bacitracin in 20 cc. of water or sodium chloride solution to give a safer coverage of the intestinal cocci and clostridia.

Penicillin and streptomycin have demonstrated their effectiveness in the treatment of peritonitis due to a mixture of lower bowel organisms. These may be given after bowel resections in a dosage of 400,000 units of penicillin and 0.5 gm. of streptomycin twice a day, or bacitracin may be substituted for the penicillin in a dosage of 20,000 units with 0.5 gm. of streptomycin every eight hours to give a wider coverage over the intestinal cocci and clostridia.

If the cultures taken at the operative site yield organisms resistant to the antibiotics that have been used, a change should be made after 24 or 48 hours to the antibiotic or mixture of antibiotics that have been demonstrated to have the greatest activity against these particular organisms. Such treatment should be given systemically, if possible.

Before operations on the vagina, cultures should always be taken, and the sensitivities of the bacteria found should be determined. Then, during the operation, the operative field should be sprayed with the antibiotic that is most potent against the contaminating organisms.

Another important field for the prophylactic use of the antibiotics comprises civilian accident wounds, burns, and gunshot wounds. These are all contaminated, usually with a mixture of organisms. Dirty accident and gunshot wounds should always be thoroughly debrided and the debrided tissues, blood clot, dirt, and other foreign bodies sent to the laboratory for culture so the surgeon may be forearmed with knowledge of which organisms are present and their sensitivities should infection develop. Some residual contaminating organisms are always left on the surface, but they are not deep in the tissues of the wound, if it is less than four hours old. This offers the best opportunity for obtaining close contact of these organisms with some potent bactericidal antibiotics. A combination of bacitracin, 1,000 units per cubic centimeter, and 1% neomycin covers most of the organisms that may be expected in these wounds. The mixture should be sprayed liberally over the surface and into all nooks and crannies. This local application is more important than the systemic use of antibiotics in these cases. It should be remembered that the organisms are on the surface and not in the tissues, unless the wound is four or more hours old.

Wounds of the scalp, face, or hands may be closed after local application of antibiotics. In other areas, the wounds may be left open, tamponed with China silk, and packed with fine meshed gauze wet with the antibiotic mixture. If on the next day the culture report indicates a change in antibiotics, they should be applied. If the cultures show no important pathogens and the wound remains clean, a late primary or early secondary closure may be done. If the cultures reveal important pathogens, the appropriate antibiotic or combination of antibiotics may be used systemically. The wound should then be left open until the pathogenic organisms disappear from it.

4. Howes, E. L.: Topical Use of Streptomycin in Wounds, Am. J. Med. **2**: 449-456 (May) 1947.

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The contamination of burns is very similar to that of wounds except that the organisms are generally more numerous and are distributed over a larger area. Again it should be remembered that immediately after the burn, the organisms are on the surface only and that this offers the best opportunity for bringing the most potent antibiotics into contact with them. Again cultures should be taken within 24 or 48 hours to determine the organisms with which the surgeon has to deal. A mixture of antibiotics should be applied to the surface as soon as the cultures have been taken and without waiting for the culture report. The antibiotic treatment should be modified later, if necessary, according to the results of the cultures.

The contamination in burns is oftenest due to hemolytic micrococci and hemolytic streptococci and gram-negative rods of the Proteus, pyocyaneus, and coli groups. Because so many micrococci are now resistant to penicillin and because many patients are allergic to it, bacitracin is the most reliable antibiotic for the gram-positive cocci, and bacitracin, together with a mixture of neomycin and polymyxin B, is best for the gram-negative rods. Polymyxin B is added to the mixture in the treatment of burns because it is the best agent against the pyocyaneus, a common contaminant in burns. There is no danger of systemic toxicity from the local application of these drugs. If the areas are to be left exposed, a solution containing this mixture may be sprayed on the surface, or, if the burn is to be kept under pressure dressing for a time (10 days), the antibiotics may be incorporated in a water-soluble base, like carbowax, on an innermost dressing of fine meshed gauze.

One more situation in which antibiotics may be used prophylactically occurs in cases of elective amputation of an extremity for gangrene. Preliminary cultures and sensitivity tests will indicate the most potent antibiotics against the organisms present in the gangrenous lesion. It must be assumed that organisms are moving up the lymphatics to or beyond the level of amputation. It is good practice to take cultures at the level of amputation and then to spray the surface with the antibiotic indicated by the preliminary culture before closing the wound. If the infection is severe and the organisms of particular virulence, the wound should be left open until the results of the cultures from the level of amputation are known. If the cultures are negative, a delayed primary or early secondary closure may be done. If the cultures are positive, local treatment with the antibiotic should be continued and systemic treatment should be instituted because of the probability that the infection has already gone beyond the cut surface.

ACTIVE TREATMENT OF SURGICAL INFECTIONS

It goes without saying that the antibiotics will not be effective in controlling any infection unless the organism is sensitive to the antibiotic used. This sensitivity can be determined only by culture studies in the laboratory. It cannot be done by guesswork. From the previous course of the infection or the area involved, many experienced surgeons may be able to guess the most likely causative species of bacteria, but they cannot guess, with any measure of certainty, the susceptibility of the organisms to any given antibiotic.

The development of resistant strains of the common organisms, first noted by the micrococci against penicillin and recently by other organisms against all of the antibiotics,[5] makes it imperative that these tests be done. It is more important to determine the sensitivities of the organisms than to name or classify the organisms. The blood agar plate method using filter paper disks wet with the proper dilution of the different antibiotics is the simplest and most reliable, and the dilutions can be adjusted so that the results are of real clinical significance. Our laboratory routinely tests the sensitivity of every culture simultaneously against the five antibiotics most commonly used, penicillin, bacitracin, streptomycin, oxytetracycline, and neomycin. A preliminary report may be made after overnight culture. If any organisms are resistant to these five, further studies are made with chlortetracycline, chloramphenicol, polymyxin B, and erythromycin.

Two years ago we sent a brief questionnaire around to the hospitals in the New York metropolitan area to find out whether they had bacteriological laboratories equipped to do aerobic and anaerobic cultures and sensitivity tests.[6] We also asked how often surgeons requested that these tests be done for cases of infection. At that time, the replies clearly indicated that many hospitals did not have these facilities and that, even when they did have them, such tests were seldom requested. It was then the common habit of many surgeons to give penicillin at once and, if that was not successful, to add streptomycin and then one or more of the other antibiotics in turn or all of them together. Then, if there was no response, they might repeat the sequence again. At a medical meeting held at that time, many surgeons present acknowledged their own fault in this regard; some blamed their laboratories.

Today, although we have not repeated the questionnaire, we know that the situation has improved considerably. More and more laboratories have these facilities, and many surgeons now request that these tests be done. Surgeons are becoming educated to the importance and advantage of calling on and relying on the laboratory for these tests. If, however, the question, "How many surgeons routinely demand these tests for cases of infection and are satisfied with the results?" were asked one wonders how many would answer in the affirmative. Certainly sensitivity studies can be done in any laboratory with the basic facilities that every hospital should have. Surgeons should request these tests, but the laboratory should carry them out routinely, whether they are requested or not. This procedure will give the surgeon the proper basis for the choice of the most effective antibiotic in any given case.

CHRONIC AND ACUTE INFECTIONS

There is a great diversity of well-established surgical infections. Among the acute infections are furuncle, carbuncle, cellulitis, superficial abscess, deep abscess,

5. Eagle, H.; Fleischman, R., and Levy, M.: Development of Increased Bacterial Resistance to Antibiotics: Continuous Spectrum of Resistance to Penicillin, Chloramphenicol, and Streptomycin, J. Bact. **63**:623-638 (May) 1952.

6. Meleney, F. L., and Johnson, B. A.: Chemotherapy and Antibiotics in Surgical Infections, S. Clin. North America **32**: 387-403 (April) 1952.

septicemia, osteomyelitis, suppurative arthritis, tenosynovitis, suppurative lymphadenitis, cholecystitis, appendicitis, local peritonitis, diffuse peritonitis, fibrinopurulent peritonitis, and Meckel's or sigmoid diverticulitis. Chronic surgical infections may develop from any acute infection that has not responded to previous treatment. An arbitrary time division between acute and chronic cases is 30 days. Among the chronic infections are ulcers, undermining or simple and with or without vascular insufficiency, lung and liver abscesses, chronic osteomyelitis, tuberculosis, actinomycosis, synergistic infections, such as progressive bacterial synergistic gangrene, fusospirochetal infections following human and animal bites, gangrenous impetigo and amebic infections, chronic ulcerative colitis, terminal or regional ileitis, chronic diverticulitis, and many others.

It is not necessary to give details of all of these separate clinical entities here, but we may briefly describe some of the principles involved in the employment of the antibiotics and the surgical procedures in the treatment of these conditions. We would like to make a plea for surgeons dealing with infections to be bacteriologically minded and to keep in mind what and where the bacteria are involved in the process and how they can be reached and destroyed by use of both the knife and antibacterial agents. Today surgery may be obviated in many cases, and this is usually to the patient's advantage.

In acute cases, if possible, a specimen of exudate should be taken by aspiration or by incision for smear and culture before instituting any drug treatment. After the culture has been taken, however, drug treatment should not be delayed. An immediate examination and report on the smear will give some hint regarding the nature of the organism. The surgeon must use his judgment as to which antibiotic is most likely to succeed and how it can best reach the organisms. If, on the next day, the culture indicates that his judgment has been correct, the original antibiotic should be continued, but, if the culture indicates a change, that change should be made at once.

In chronic cases, a careful bacteriological analysis should be made before starting treatment because there is usually a mixture of organisms present that have resisted previous antibiotic treatment. In established infections, the organisms are not merely on the surface but deep in the tissues, possibly in thrombosed blood vessels or in the blood stream. In such cases, the local application of the antibiotic may not contact the organisms; the antibiotic should then be given systemically in such doses and at such frequent intervals that it will reach the spreading periphery of the infection. In many established infections, however, local application is sufficient and the antibiotic can be brought into contact with the organisms in much higher concentration than by means of systemic treatment and without any damage to the local tissues. In this respect, the antibiotics such as penicillin, bacitracin, polymyxin B, streptomycin, and neomycin are far superior to the sulfonamides.

The toxic effects of bacitracin given systemically, which were produced by the early deep-tank method of manufacture, have largely been overcome. The preparations that are now available for parenteral use are effective and safe, if given intramuscularly in a dosage of not more than 20,000 to 25,000 units every six or eight hours and if there is a daily fluid intake of at least 2,500 cc.[7] Neomycin cannot be given systemically without fear of toxicity. Polymyxin B can be given safely with due regard to dosage and should be employed in pyocyaneus septicemia and in resistant cystitis and pyelonephritis due to the same group of organisms, if they are susceptible to it by in vitro tests.

The body cannot develop any immunity against most of the organisms causing surgical infections, but it can against many organisms causing medical infections. This immunity often plays a part in the recovery from medical infections.

It is of interest and of some importance that if chlortetracycline or oxytetracycline fails to control the infection, the use of the other is not likely to succeed, because the susceptibilities of organisms run fairly parallel with these two antibacterial agents. If resistance develops to one of them during the course of treatment, that organism is also resistant to the other.[3]

It has been demonstrated that penicillin and bacitracin may be injected directly into the center of furuncles and carbuncles and that they often stop the bacterial action abruptly and check the further spread of the necrosis, if the causative organism is sensitive. Both of these antibiotics seem to hasten the liquefaction of slough, which of course must be removed either by incision and drainage, by spontaneous discharge, or by absorption. With carbuncles, if there is a narrow zone of induration around the necrotic center, injection into the center is sufficient to cause resolution because it permits a certain amount of absorption into the periphery. If there is a wide zone of induration and a small central area of necrosis, the antibiotic with procaine hydrochloride (Novocaine) or butethamine (Monocaine) hydrochloride may be injected around the periphery with rapid resolution of the process. In the treatment of abscess cavities, the pus may be aspirated and the antibiotic instilled and reaspirated mixed with pus. This procedure should be repeated, if and when there is a reaccumulation of pus. Often the whole process resolves in three or four days and the surgical procedure of incision is frequently obviated. If there is a wide zone of cellulitis or other indications of peripheral spread or sepsis, the systemic administration of the antibiotic is indicated.

In cases of surgical infection caused by the hemolytic Streptococcus, the hemolytic Micrococcus (Staphylococcus) aureus, and organisms of the coli, Proteus, and Pseudomonas groups, septicemia may be present; this means that the bacteria may be recovered from the blood stream. In such cases, it behooves the surgeon to seek, to remove, if possible, or drain the distributing focus, and to give systemically that antibiotic to which the organism is most sensitive. It is particularly important in cases of acute osteomyelitis that the most potent antibiotic be given early, within four days, to prevent the breakdown of the bone and its very unfortunate sequelae.

7. Meleney, F. L.; Johnson, B. A., and Teng, P.: Further Experiences with Local and Systemic Bacitracin in the Treatment of Various Surgical and Neurosurgical Infections and Certain Related Medical Infections, Surg., Gynec. & Obst. 94: 401-425 (April) 1952.

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Purulent collections in joints or in the pleural cavity may also be removed by aspiration and the infection controlled by the instillation of penicillin or bacitracin with reaspiration. This may be repeated as often as there is reaccumulation of exudate. Again in such cases surgery may often be obviated.

In well-established infections in operative or accidental wounds and burns, local treatment with the most potent antibiotic or mixture of antibiotics is often sufficient, but, if there is evidence of spread into the deep tissues, antibiotics must be given systemically. With respect to the gram-negative bacilli, the broad spectrum antibiotics are often the most effective.

In what we have said above, it is seen that the availability and effectiveness of the various antibiotics have modified some of our former fundamental principles in the treatment of surgical infections, but acute surgical infections within the peritoneal cavity should still be governed by the same general rules that have been good for a long time, namely, early operation and the removal of the offending focus, if that is possible. Operation gives the surgeon a clear picture of what he is dealing with, and cultures can then determine the nature and susceptibilities of the offending organisms.

In many instances, chronic surgical infections have been inadequately and improperly handled without a proper bacteriological study or without treatment with an antibiotic potent against the causative organisms. One might go as far as to state that today no acute surgical infection should ever become chronic while under the intelligent care of a competent surgeon. In many cases, the surgical procedures have been inadequate, and there may be necrotic tissue still present in the focus of infection. Almost invariably secondary organisms have had an opportunity to get into the area of infection and may be playing a synergistic role. These cases require a thorough study of the bacterial flora in the infected area and tests for susceptibility of all of the organisms found to all of the available antibiotics. Thereafter these patients require the careful application of the most potent antibiotic or mixture of antibiotics both locally and systemically. With some of these chronic infections, that is all that is necessary to turn the tide and start wound healing, but many of these cases first require surgical removal of the necrotic tissue. This is particularly necessary in chronic osteomyelitis, which demands the excision of all of the grossly diseased bone followed by the local application of the indicated antibiotics, preferably those of the bactericidal group. This treatment should be continued daily until healing begins and permits either a secondary closure or a skin graft.

SYNERGISM AND ANTAGONISM

When faced with a fulminating acute infection or a long-standing chronic one, some surgeons give two or three antibiotics as a shotgun remedy without any consideration of bacterial cultures or sensitivity test and without a thought concerning the possibility of antagonism of one antibiotic toward another. The surgeon often excuses himself by saying, "If one antibiotic doesn't stop the infection, one of the others will." This practice is certainly to be condemned as being unscientific, usually ineffective, and often harmful.

When primary cultures and sensitivity tests show a single organism and a single potent antibiotic out of five or more tested, that antibiotic should be used alone. If there is a mixture of organisms, as is so often the case in chronic infections, the susceptibility of each one should be tested and the most potent antibiotic used against each organism provided the antibiotics are not antagonistic to one another. If none of the antibiotics is effective by routine tests, the concentration can be increased in liquid mediums and the minimal inhibiting concentration can be determined. At times synergism of two antibiotics may be demonstrated by combining fractions of each of the minimal inhibiting concentrations. We believe that one criterion for demonstrating synergism should be that one-fifth plus one-fifth (or less) of each of the minimal inhibiting concentrations causes inhibition of growth. The two antibiotics may be said to have a synergistic action. If one-half plus one-half of the minimal inhibiting concentrations causes inhibition, it is considered an additive effect. If the combination requires more antibiotic for inhibition than the minimal inhibiting concentration of each one alone, there is antagonism.

The terms synergism and antagonism have been used for many years. In 1948, Eagle and Fleischman reported the remarkable synergistic action of penicillin and bacitracin in syphilis in experimental rabbits.[8] We have demonstrated, and reported in 1950, both in vitro and in vivo synergism of penicillin and bacitracin.[9] Jawetz and his co-workers have recently made many laboratory and clinical observations on this subject.[10] They find that synergism often exists between two of the bactericidal, or group 1, antibiotics (penicillin, bacitracin, streptomycin, polymyxin B, and neomycin) and between antibiotics of the bacteriostatic, or group 2, antibiotics (chlortetracycline, oxytetracycline, and chloramphenicol). However, antagonism often results, if a member of group 2 is combined with a member of group 1. This does not always hold true and cannot be predicted with certainty. It depends a great deal on the susceptibility or resistance of the organisms.[11] However, it should be kept in mind when antibiotic combinations are used clinically. Combinations of the two groups should be avoided unless synergism has been demonstrated in vitro. Further study is required on this important problem, and it will need to be continued as new antibiotics become available.

SUMMARY AND CONCLUSIONS

The natural course of surgical infections may be profoundly altered or brought to a complete standstill by the use of the appropriate antibiotic or combination of antibiotics in addition to the proper surgical procedure. Many times surgery may be completely obviated or its extent curtailed.

8. Eagle, H., and Fleischman, R.: Therapeutic Activity of Bacitracin in Rabbit Syphilis and Its Synergistic Action with Penicillin, Proc. Soc. Exper. Biol. & Med. **68**: 415-417 (June) 1948.

9. Johnson, B. A., and Meleney, F. L.: Studies on the Synergism Between Bacitracin and Penicillin: Correlation of in Vivo with in Vitro Results, Ann. New York Acad. Sc. **52**: 42-49 (Aug.) 1950.

10. Jawetz, E.: Therapeutic Use of Combinations of Antibiotic Agents, Cornell Conferences on Therapy, New York J. Med. **53**: 1228-1233 (May) 1953.

11. Klein, M., and Schorr, S. E.: The Role of Bacterial Resistance in Antibiotic Synergism and Antagonism, J. Bact. **65**: 454-465 (April) 1953.

Successful treatment requires, on the part of the surgeon, the knowledge of the natural occurrence of bacteria in relation to the body, their potentialities and predilections, their behavior after gaining a foothold in the body, and the proper methods and timing of certain surgical procedures. Of equal if not greater importance for success in treatment is a knowledge of the causative and associated organisms and their susceptibility to the available antibiotics and the proper methods for their application. Our recent experience in the use of antibiotics and surgery in the treatment of surgical infections is outlined.

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PHARMACOLOGICAL TREATMENT OF AGED PATIENTS IN A STATE MENTAL HOSPITAL

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Improvement in medical care and general living conditions has definitely lengthened the average span of human life. Each year a greater percentage of the population reaches advanced ages, and statistics indicate that this trend will continue. Consequently there are constantly increasing numbers of persons subject to degenerative changes, especially in the central nervous system. Therefore, there has been an ever increasing demand for admission of aged patients to private and public mental institutions, and at the present time more than one-third of all persons first admitted to public mental hospitals in the United States are over 65 years of age. The magnitude of the important problem posed by this group needs no further emphasis, but it becomes even clearer if one considers that, for each person whose condition requires care in a mental hospital, there must be several others who can be cared for at home and who are not admitted to such a hospital. Out of necessity, therefore, extensive interest has been created in the problem of the aged patients, and consequently much attention has been given to the emotional problems of the aged and the aging, and new methods and ways are being found to deal with them.

In certain of these aged persons, impairment in the central nervous system is severe enough to produce serious emotional disturbances, paranoid delusions, advanced deterioration, and difficult behavior problems. These patients undoubtedly need and deserve the protection and the modern psychological and psychiatric treatment methods that are provided in an up-to-date psychiatric hospital.

Recently much progress has been made in the treatment of psychotic reactions in the aged. The previously held attitude of therapeutic nihilism for this group was based on the erroneous belief that senile organic changes described as both progressive and irreversible were the sole causes of the mental symptoms. This belief has been entirely abandoned, since more recently pathological studies have shown that there is no direct correlation between the intensity of mental symptoms and the severity of the pathological changes. In fact, many of the patients with the severest neuropathological changes were found to be free of mental symptoms during their lifetime, as reported by Rothschild [1] and others. Furthermore, attention was drawn repeatedly to the high incidence of so-called functional types of psychotic reactions that first developed late in life and that were not the result of irreversible pathological brain changes. It was also found not to be uncommon for major mental disorders to occur first in old age. Clow,[2] for instance, among 100 patients with psychosis accompanied by cerebral arteriosclerosis, found 61 who had previously in their adult years showed more or less minor symptoms of mental illness characterized mainly by sexual maladjustment and psychopathic behavior. This, then, resulted in a new therapeutic approach. In addition to other psychological and physiological methods, convulsive therapy is being more and more utilized in the treatment of aged psychotic patients, after having been proved to be a relatively safe and successful procedure. An increasing number of favorable reports of this therapy have appeared in the literature, among them reports by Robinson,[3] Bennett,[4] Wilbur and Fortes,[5] and more recently by myself.[6]

On the other hand, however, the majority of these aged patients show only mild memory defects, slight confusion, and the somewhat more exaggerated deterioration characteristic of the aging process. Their medical care and disposition presents much more complicated problems than those of the aforementioned group, and unfortunately are not solved adequately at the present time. Although the public mental hospitals have been called on to care for an increasing number of such older patients, this group of elderly patients presents a problem in itself within the institution. It has been shown, for instance, that in the state hospital these patients individually do not present any burden, but rather do collectively because of the ever increasing number of them admitted. Their individual prognosis is definitely poor, for very few of these patients can ever hope to be discharged, and within the first 12 months almost one-half of them have died. In fact, the highest death rate occurs within the first month of admission, in spite of the fact that on admission their physical health is good and average for their ages, and in spite of the probably much better medical and nursing supervision than a person of that age could expect in his own home or even in a nursing home or county farm. They are, however, as has been shown, called upon to make an entirely new emotional adjustment in a strange environment. The adjustment at this age, because of their limited mental capacity for grasping new situa-

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tions, seems almost impossible. A vicious cycle is thus set in motion as they become more emotionally disturbed and that in turn there is a detrimental, almost fatal, effect on their physical health.[7]

Thus, during recent years, various studies have appeared in the literature dealing with newer methods of treatment for this group. The methods include, to name a few, the possibility of home care for the aged, the creation of special institutions, the improvement of nursing care, the application of newer psychological treatment methods, meeting of dietary requirements, and finally therapy with various drugs.

The role of anoxia in disease is being recognized more and more, and since it has been found that the brain is also particularly sensitive to oxygen lack, it is not surprising that anoxia may lead to mental disturbances. Houston [8] in 1949 stated, "The mental signs of anoxia may be subtle and easily mistaken for primary neurologic disease. Mental confusion, emotional lability, errors in judgment, inability to concentrate, headache, or gross tremors are frequently caused by oxygen lack alone and may be a principal evidence of its presence. These signs and symptoms are often seen in elderly persons with arteriosclerosis, in patients with chronic pulmonary disease, anemia, carbon monoxide poisoning, and other conditions that cause chronic low-grade, tissue anoxia." Freyhan and co-workers,[9] using the nitrous oxide technique, studied cerebral blood flow and cerebral metabolism in patients with senility and cerebral arteriosclerosis. They concluded that their data as a whole strongly suggest that the senile psychoses, including those associated with cerebral arteriosclerosis, are associated with and are probably the result of a significant reduction in cerebral oxygen utilization caused by increased cerebrovascular resistance and the resultant significant reduction in blood flow through the brain. However, it should be mentioned at this point that elderly, nonpsychotic persons also have relative cerebral anoxia and that no correlation could be made between readings obtained and mental symptomatology.

Consequently, a great deal of importance was attached to cerebral anoxia as the factor responsible for the mild mental symptoms in the aged, and various therapies were introduced with the ultimate goal of correcting this factor. On the basis of experimental work with respiratory enzymes, it was found that cytochrome C, for instance, might be employed in the problems of tissue anoxia, acute and chronic, and to meet many cellular needs, especially during attempts at regeneration of nerve cells. It was argued that these conditions would seem to be outstanding in the presenile and senile brain, with or without arteriosclerosis, where ganglion cells undergo the typical changes of involutional atrophy and degeneration with interactions of parenchyma and neuroglia that are subject to much variation. On the basis of this reasoning, Garnett and Klingman [10] in 1949 reported the results of a biochemical experiment with cytochrome C in 17 patients with presenile, senile, arteriosclerotic, and involutional states. Their results showed that, of the 17 patients observed, 11 were thought to show clinical improvement and 6 to show none during and after injections of cytochrome C. The clinical improvement in their series was noted in a majority of cases in regard to memory, orientation, irritability, interest, confusion, and behavior. They observed only slight changes in the electroencephalographic recordings and stated that these changes may be insignificant. Psychometric examinations showed qualitative improvement in keeping with clinical improvement and a trend toward higher scores. On the other hand, Forster [11] in 1951 reported the results of treatment with cytochrome C in cases of senile and arteriosclerotic dementia and stated that it was not possible to demonstrate any significant improvement in the treated group compared to the control group that received injections of normal saline solution.

Pentylenetetrazol (Metrazol), a synthetic organic tetrazole compound, has long been effective in respiratory and circulatory stimulation. Pharmacologically it is said to exert an intense stimulating action on the central nervous system. It acts primarily on the higher centers of the brain, particularly on the respiratory, vasomotor, and vagal centers of the medulla, but all parts of the cerebrospinal axis are stimulated to some degree. Its analeptic action is said to be most evident when the higher centers are depressed owing to narcotic drugs, including the barbiturates and alcohol, or to illness or to old age.[12]

On the basis of these facts, Chesrow and co-workers [13] argued that "one might expect that metrazol by stimulating the respiratory center in the aged would improve pulmonary ventilation and indirectly the circulation and so help to overcome the anoxia frequently present in the aged, the depressed and the fatigued. At the same time the analeptic action of the drug and its ability to increase nerve impulse transmission should act as a general tonic so that the patient might well have an increased sense of well-being, be less depressed and perhaps also less confused." They gave pentylenetetrazol orally in arteriosclerosis associated with senility and selected for their study 32 cases of advanced arteriosclerosis with definite evidence of mental confusion. Pentylenetetrazol was given orally in an average dose of 1 or 2 tablets four times a day, and the authors reported excellent results in 4 cases, marked improvement in 8, fair improvement in 10, some improvement in 4, and no improvement in 6 cases. They concluded that "judging from this rather small series of cases metrazol is an effective and safe analeptic and of definite value in geriatric practice." Similar favorable results with the oral use of pentylenetetrazol were reported by Fong [14] at the gerontological meeting in September, 1952, at Washington, D. C. Dr. Fong chose very disturbed, almost psychotic patients, and 48% of them showed definite improvement, especially in becoming more amenable to ward discipline. Suter [15] and Linden and Courtney [16] were also able to confirm the beneficial effects of pentylenetetrazol given orally to mentally confused persons. More recently Swenson and Grimes [17] reported on the oral use of pentylenetetrazol, especially as it affects behavior, in 25 hospitalized patients. They found no statistically significant differences in a comparison of the pretreatment and post-treatment rating, but stated that subjective reports of patients and ward personnel indicated that certain observable changes may have occurred. Some of the patients receiving pentylenetetrazol slept better, were more active on the ward, and

displayed less antisocial behavior. They claimed that further study using different rating techniques and larger doses of pentylenetetrazol seems indicated.

Following the successful use of nicotinic acid in relieving mental symptoms of pellagra, this drug soon was applied in the treatment of a number of psychiatric syndromes, particularly organic psychoses of varied etiology. Cleckley, Sydenstricker, and Geeslin [18] obtained beneficial results from the use of nicotinic acid in a group of patients with organic psychoses who showed no typical signs of pellagra but did present some evidence of malnutrition. Later Sydenstricker and Cleckley [19] reported that nicotinic acid had proved effective in the treatment of another group of patients with organic psychoses, two-thirds of whom were in the senile or presenile age range and in none of whom was there any suspicion of pellagra. On the basis of their studies, these workers concluded that a therapeutic trial with nicotinic acid was indicated in confusional psychosis attributed to cerebral arteriosclerosis or senility, or in toxic psychosis, exhaustion delirium, and other confusional psychoses of doubtful etiology. More recently Caldwell and Harwick [20] and Lehmann,[21] among others, expressed the opinion that nicotinic acid is of value in the treatment of organic psychosis attributed to cerebral arteriosclerosis or senility. The rationale of this treatment is based upon the now generally accepted hypothesis that nicotinic acid may produce its beneficial effect in many confusional states by means of cerebrovasodilatation, as originally advanced by Moore [22] and Aring and co-workers.[23] More recently, however, Scheinberg [24] exploring other scientific techniques of investigation, concluded that nicotinic acid does not cause cerebral vasodilatation. It was also argued that many aged persons also have evidence of deficiency of nicotinic acid so that they can benefit from its administration. More recently Gregory [25] determined the efficacy of nicotinic acid in psychoses of senility. He studied 54 patients and found that the prognosis with nicotinic acid therapy appears to be correlated with age; the younger the patient the better his chances of recovery. He found that marked improvement occurred in about 50% of patients under 65 years of age and in only about 10% of those over 65 years of age. He also stated that nicotinic acid is most beneficial in confusional states and psychoses of recent onset, and that it must be administered promptly because reversible changes in cellular function are followed quite rapidly by irreversible structural changes. Thus, on the basis of this study, Gregory suggests that nicotinic acid may be of more benefit in prophylaxis than in cure, since according to him some deficiency of nicotinic acid is believed to be one of the etiological factors involved in the development of psychoses in the aged.

Histamine, because of its vasodilatory properties, has also been used in cases of cerebral arteriosclerosis with the hope of improving the cerebral circulation; however, Taylor [26] was unable to produce any beneficial changes with its use. More recently Moore and co-workers [27] reported on the combined histamine-nicotinic acid therapy and claim excellent results with this method. They stated, "We believe intravenous histamine-nicotinic acid dilation therapy actually improves the function of physiologically impaired or non-functioning brain cells. Whether this is a result of increased cardiac output, increased vasodilatation of cerebral vessels, increased capillary permeability, or an actual physiological action on the cells we do not know." They claim that 23 of 24 patients were greatly improved; 21 were able to leave the hospital, many of them being engaged successfully in various types of work.

Tolazoline (Priscoline) given in 25 mg. doses four times daily for four weeks has also been employed in the treatment of confusional states and psychotic reactions among the aged.[28] However, the report indicates that the psychotic symptoms of patients receiving tolazoline were not benefited by the medication.

Of the other pharmacological treatment methods applied for the mildly confused and deteriorated aged, administration of steroid hormones has been used with more or less success.[29] Other methods include stimulatory drugs such as *dl*-amphetamine sulfate (Benzedrine), *d*-amphetamine sulfate (Dexedrine), caffeine and ephedrine, as well as the various vitamins and proteins. However, all these produced little, if any, improvement.

The present study, then, concerns itself with the pharmacological treatment of the aged, particularly those with only memory defects, confusion, and deterioration in the absence of more serious emotional and psychiatric disturbances. This study was undertaken with the aim of finding a therapeutic regimen for this large group of institutionalized patients that is not only practical but also simple and safe. For this reason stimulatory, vasodilatory, and enzymatic drugs were investigated.

MATERIAL AND METHOD

Thirty male patients were used in this study, and these patients served as their own controls. Their ages ranged from 61 years of age to 88 years of age, the average age being 74 years. The patients were selected because of the presenting clinical picture of marked memory defect, confusion and deterioration, and mild behavior disorders, but without overt symptoms of serious emotional and psychiatric disturbances. These patients fall into various diagnostic categories, more than two-thirds having a diagnosis of either arteriosclerosis or senility. The exact diagnostic classification of the 30 patients is as follows:

Chronic brain syndrome associated with arteriosclerosis with behavioral reaction	12
Chronic brain syndrome associated with senile brain disease with behavioral reaction	8
Chronic brain syndrome associated with senile brain disease associated with psychotic reaction	1
Chronic brain syndrome associated with circulatory disturbance with behavior reaction	2
Paranoia	1
Paranoid state	1
Schizophrenic reaction, paranoid type	4
Manic depressive reaction, depressed type	1
Total	30

As can be seen, some of the patients fall within the diagnostic classification of functional disorders such as schizophrenia of long-standing. These were purposely included because in most of them the so-called senile changes overshadowed their original mental disturbances, and their overt behavior was entirely in correspondence with their aging process and not with the symptomatology of their original mental disorder. The average length of stay in the hospital of this group of patients was 7 years, with the shortest stay 9 months and the longest over 40 years.

Cytochrome C parenterally, pentylenetetrazol orally, nicotinic acid orally, either alone or in combinations of two or three, and placebos identical in appearance and given by the same route were administered to the same group of patients. Cytochrome C was administered according to the method described by Garnett and Klingman. After a negative skin test, 1 cc. of cytochrome C was given intravenously. On the following day 2 cc. were given intravenously, on the third day 3 cc., and thereafter 5 cc. daily for a total of 15 days. Pentylenetetrazol, on the other hand, was given orally in tablet form, the dose being two tablets three times a day, or a 24-hour total of 9 grains (0.6 gm.) for a period of 30 days. Nicotinic acid was also given orally, the dosage being 100 mg. three times a day for 30 days. Placebos identical in appearance and administered by the same route were given for a period of three weeks in between the various courses of drug therapy. It was then decided to combine the various drugs, and for 21 days the patients were given an elixir of pentylenetetrazol and nicotinic acid. This elixir per drachm contained 3 grains (0.2 gm.) of pentylenetetrazol and 100 mg. of nicotinic acid in a vehicle of compound pepsin elixir. One drachm of the elixir was given three times daily. In other words, each patient received 0.6 gm. of pentylenetetrazol and 300 mg. of nicotinic acid in a 24-hour period. Finally, for a period of 21 days 5 cc. of cytochrome C were given daily in addition to the daily dose of elixir containing pentylenetetrazol and nicotinic acid.

Complete physical and neurological examinations, electroencephalograms, chest roentgenograms, complete blood counts, urinalyses, and determinations of the sedimentation rate, the nonprotein nitrogen, creatinine, icteric index, lactic acid, and fasting blood sugar were done prior to the start of the investigation, at the end of each period of drug as well as placebo administration, and following the termination of the investigation. Psychometric examinations using the verbal scale of the Wechsler-Bellevue, both forms 1 and 2, as well as electroencephalographic tracings were made at the same intervals. The chest roentgenograms were interpreted by the consulting roentgenologist, electrocardiograms by the consulting cardiologist, and the electroencephalograms by the staff encephalographer. Psychometric examinations were conducted by graduate students of the department of psychology of Washington State College, Pullman, Wash. None of these interpreters had any knowledge of the type or amount of therapy being administered to these patients. Daily clinical observations were made by the psychiatric aides, and they were recorded on a revised Malamud-Sands Worchester Rating Scale. The original Worchester Rating Scale was used by the supervisor, who checked the patients' behavior twice weekly, and also by the ward physicians, who checked the patients' behavior once weekly. These observers were aware that this particular group of patients were subject to an experimental investigation; none of them, however, had any knowledge of the type or amount of therapy being given. It should also be mentioned that these patients remained in the same ward environment as their fellow patients who did not participate in the study, and their daily routine during the testing periods was the same as previously. No other medicament except an occasional sedative at bed time was administered.

The original Worchester Rating Scale as modified by Malamud and Sands was modified for use by the psychiatric aides. Of the 19 points to be checked on the original scale, only 12 of these were utilized by us in a simplified form as shown in table 1.

Originally the study was started with 30 patients, but one of the patients died suddenly of coronary occlusion during the investigation, so that the study was completed with only 29 patients. Psychological testing could be carried on in only 24 of the 29 patients and in only 20 of the 29 patients was it possible to obtain a complete series of satisfactory electroencephalographic tracings. The daily, twice weekly, and weekly observations as well as the laboratory tests, chest roentgenograms, and electrocardiograms were made on the complete series of 29 patients.

TABLE 1.—*Revised Malamud-Sands Worchester Rating Scale**

Appearance	Neat
	Careless
Personal Habits	Able to Attend to Needs
	Has to be Assisted
General Activity	Active
	Quiet
Sociability	Mixes With Others
	Does Not Mix
Attention	Alert
	Dull or Indifferent
Mood	Elated
	Even
	Depressed
Feelings	Too Sensitive and Irritable
	Easy Going
	Too Indifferent
Speech	Spontaneous
	Uncommunicative
Memory	Good
	Fair
	Poor
Work	Willing
	Disinterested
Eating Habits	Spontaneous Eating
	Feeding Problem
Sleep	Restful
	Restless

* One factor for each category was to be checked; that is, the factor that most closely described the patient and his activity.

RESULTS OF STUDY

The results of this study are summarized in table 2. From this table it can be seen that the most important changes occurred following the administration of the elixir containing pentylenetetrazol and nicotinic acid. This elixir produced a marked improvement in the behavior of the patients as seen on the rating scale, a better performance on psychological tests, an improvement in the physical health of the patients through gain in weight, and restoration to normal of previously abnormal lactic acid values of the blood. In addition, some of the electroencephalograms that were abnormal at the beginning of the study returned to normal. Other important findings shown on this table indicate that, following administration of cytochrome C, there was a drop in the blood count and hemoglobin that produced a mild to moderate secondary anemia; also the behavior of these patients as seen on the revised Malamud-Sands Worchester Rating Scale seemed slightly deteriorated as compared to the basic evaluation. On the other hand, following the administra-

tion of (1) pentylenetetrazol orally, (2) cytochrome C (3) nicotinic acid orally, (4) the combination of cytochrome C plus the elixir of pentylenetetrazol and nicotinic acid, and (5) the administration of placebos, no significant clinical or laboratory changes occurred.

The influence of the various drugs on the different behavior characteristics, as seen on the revised Malamud-Sands Worchester Scale, is shown in table 3. It should be mentioned here that the scoring of all three independent observers corresponded in about 85% of the cases, so that the findings given on table 3 are the pooled results of these independent observations. From this table it can be seen that the improvement in the rating scale following administration of the elixir of pentylenetetrazol and nicotinic acid was present in almost all checked factors, while the other drugs produced no or very variable and only insignificant changes.

The chart indicates the percentage of patients showing improvement in each of the 12 behavior factors following the administration of the elixir of pentylenetetrazol and nicotinic acid. It can be seen from this chart that the greatest improvement occurred in what is described as feelings. Seventy per cent of the patients who were previously described as too sensitive or irritable became easy going following the administration of the elixir. Fifty-two per cent of the patients who previously did not mix well with others became more sociable and mixed well with other patients. After this treatment 48% of the patients who previously had to be assisted with their personal needs were able to take care of their personal hygiene and to attend to their personal needs alone. In general appearance 41% improved, and they became neat while previously they were careless. Thirty-eight per cent became more alert, and 31% showed improvement in both memory and general activity. The factors least affected were what is described as interest in work and eating habits; only 14% of those who had been feeding problems improved and were able to feed themselves spontaneously.

Lactic acid values, which were abnormal in over 85% of this group before the investigation was started, became normal in all but one of the patients following the administration of the elixir. This might be due to the improvement in behavior that resulted in greater activity and thus indirectly affected the circulatory system. On the other hand, only slight and insignificant changes occurred in the lactic acid values after the administration of pentylenetetrazol, the elixir of pentylenetetrazol and nicotinic acid, and cytochrome C. After the administration of the elixir of pentylenetetrazol and nicotinic acid, all patients subjectively stated that they felt much better physically, and this was objectively confirmed by the gain in weight, ranging from 2 to 8 lb. (907 to 3,629 gm.) in over 75% of the patients. On psychological examinations with the Wechsler-Bellevue there was an average gain of 6 points in the intelligence quotient following the administration of the elixir of pentylenetetrazol and nicotinic acid. This gain was probably due to the increase of attention and improvement of feelings of the patients. They were able to concentrate better on the tests and took more interest in them. This gain becomes even more marked when this group of patients was divided into those suffering from long-standing functional psychoses such as types of schizophrenic reactions and those suffering from cerebral arteriosclerosis or senility. In the latter group, the so-called organic group, there was an average improvement in the intelligence quotient of 9 points, while the so-called functional group showed only an average improvement

TABLE 2.—*Changes* Observed After Administration of Drugs and Placebos*

	Cytochrome C	Pentylenetetrazol Orally	Nicotinic Acid Orally	Elixir †	Cytochrome C and Elixir †	Placebo
Physical findings	0	0	0	++	0	0
Electrocardiogram	0	0	0	0	0	0
Chest roentgenograms	0	0	0	0	0	0
Electroencephalograms	0	0	0	+ to ++	0	0
Complete blood count	− to − −	0	0	0	±	0
Sedimentation rate	±	±	±	±	±	±
Nonprotein nitrogen	0	0	0	0	0	0
Creatinine	0	0	0	0	0	0
Icteric index	± to −	0	±	±	±	±
Lactic acid	0	+	0	+++	± to +	0
Blood sugar	0	0	0	0	0	0
Urine	0	0	0	0	0	0
Clinical observation ‡	−	+	± to +	+++	0	0
Psychometric evaluation	0	0	0	++ to +++	0	0

* 0 = no change; + = slight improvement; ++ = moderate improvement; +++ = marked improvement; ± = too variable; − = slight decline; − − = moderate decline; − − − = marked decline.
† The elixir of pentylenetetrazol and nicotinic acid.
‡ Based on the Malamud-Sands Worchester Rating Scale.

TABLE 3.—*Behavior Changes* Following Administration of Various Drugs and Placebos as Seen on the Revised Malamud-Sands Worchester Rating Scale*

	Cytochrome C	Pentylenetetrazol	Nicotinic Acid	Elixir †	Cytochrome C and Elixir †	Placebo P
Appearance	0	0	0	+	0	0
Personal Habits	−	0	0	+	−	0
General Activity	0	+	+	+	+	0
Sociability	−	+	0	+	−	0
Attention	−	+	0	+	0	0
Mood	−	0	+	+	0	0
Feelings	−	−	0	+	0	0
Speech	−	0	0	+	0	0
Memory	0	0	0	+	0	0
Work	0	0	0	0	0	0
Eating Habits	−	+	0	0	0	0
Sleep	0	0	0	+	0	0

* + = better; 0 = no change; − = worse.
† The elixir of pentylenetetrazol and nicotinic acid.

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of 2 points. This might be due to the fact that in the functional group deterioration had occurred because of the long duration of the illness that seemed to a certain point irreversible.

As mentioned previously, a complete series of satisfactory electroencephalographic tracings was obtained on only 20 patients of this group. Thirteen, or 65%, of these tracings were considered normal and were not affected by any of the drugs and placebos. This is approximately the same incidence of normal electroencephalograms among arteriosclerotic and senile persons as has been reported in the literature.[30] Seven, or 35%, of the total were abnormal. Three, or 15%, of the total group, or 43% of the abnormal electroencephalograms became normal following the administration of the elixir of pentylenetetrazol and nicotinic acid, while four remained unchanged. The abnormalities in these three tracings, which were of the paroxysmal type, disappeared following the administration of this elixir.

No correlation could be made in regard to the age of patients; in other words, the improvement obtained following the administration of the elixir was present regardless of the age of the individual patient. This would be somewhat in variance with the findings of Gregory,[25] who found that the improvement with nicotinic acid is closely related to the age of the patient. However, it should be mentioned that this author used nicotinic acid alone and not in combination with pentylenetetrazol.

SUMMARY AND CONCLUSION

The value of various stimulatory, vasodilatory, and enzymatic drugs in the treatment of aged persons hospitalized in a state hospital for the mentally ill was studied. It was found that the greatest improvement for this type of patient was obtained with a combination of pentylenetetrazol (Metrazol) and nicotinic acid. These drugs were combined in an elixir containing per drachm 3 grains (0.2 gm.) of pentylenetetrazol and 100 mg. of nicotinic acid with compound pepsin elixir as the vehicle. It was given in doses of 1 drachm three times a day. This elixir produced physical improvement in the patients both objectively and subjectively, produced a marked improvement in their behavior and a better performance on psychological testing with an increase in the intelligence quotient, restored to normal previously abnormal blood lactic acid values, and restored to normal some of the previously abnormal electroencephalographic tracings. Cytochrome C on the other hand, which previously has been said to be of value for this type of patient, has not shown beneficial effects, at least in the doses administered in this study. In fact, it was found that, after administration of cytochrome C, there was not only a slight deterioration in the patients' behavior but also a tendency toward secondary microcytic anemia.

On the basis of this study it is, therefore, felt that the combination of pentylenetetrazol (an analeptic) and nicotinic acid (a vasodilator) is of value in the treatment of aged patients hospitalized in an institution for the mentally ill. It is particularly helpful for those with only mild memory defects, confusion, and deterioration in the absence of more serious emotional and psychiatric disturbances. It seems especially helpful in combating symptoms of abnormal behavior, and those are the symptoms that are most objectionable to the family members and relatives. On the other hand, symptoms pertaining to intellectual impairment are not combated so effectively with this combination of drugs. This might be due to the fact that intellect and memory are first to suffer, while personality and behavior changes occur later. Thus it may be assumed that the former phenomena depend on more definite organic changes that may be irreversible, while the latter symptoms, those dealing with impaired behavior, to some extent may still be reversible.

This combination has proved safe and simple as well as practical and inexpensive, and thus can be used without hesitation on an ambulatory basis. With its use it should be possible to ease the burden of caring for the mildly confused and mildly deteriorated aged patients in public and private psychiatric institutions. Thus a smaller proportion of hospital personnel and budget would be needed for what previously amounted only to custodial care of this group of patients. This saving would eventually enable the mental hospital to return to its primary function, namely, the treatment and rehabilitation of younger mentally ill patients, instead of becoming a purely custodial organization for the aged. Since many of the aged persons studied showed only the commoner evidences of simple deterioration, only modification of the conditions for which this elixir has proved successful was required. Many of these patients, with the aid of this elixir, or possibly similar acting drugs would therefore not inevitably have to be committed to psychiatric institutions and could be permitted to live in the community with safety and without harm to others.

Percentage of patients studied in whom changes according to the Revised Malamud-Sands Worchester Rating Scale were observed.

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ERYTHROMYCIN IN LOCAL TREATMENT OF CUTANEOUS BACTERIAL INFECTIONS

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Erythromycin, discovered by McGuire and his associates [1] in 1952, is a new antibiotic produced by a micro-organism (identified as a strain of Streptomyces erythreus) that was isolated from a soil sample collected on the Island of Panay, Philippine Islands. This antibiotic is white, crystalline, soluble in water to the extent of about 2 mg. per milliliter, and highly soluble in some organic solvents, such as alcohol and acetone. It is a basic compound with an empiric formula that is thought to approximate $C_{39}H_{73}NO_{13}$; there is no benzene ring structure in the formula. Stability data indicate that the dry crystalline compound is stable at room temperature for at least a year, but solutions of the antibiotic are comparatively unstable. The best stability is achieved with low temperature and neutral pH. At room temperature with a pH of 7, 86% activity remained after a storage period of 24 hours, whereas no activity remained after the same period of time with a pH of 4.[2]

Erythromycin is effective by mouth, and currently this is the only systemic route of administration. The recommended dosage schedule for adults is from 300 to 400 mg. every eight hours and for children from 6 to 8 mg. per kilogram of body weight every six hours.

The original pharmacological investigation of the drug by McGuire and co-workers [1] indicates that erythromycin has a comparatively low toxicity in animals and does not affect parenchymatous organs significantly. There was no evidence of eighth nerve damage in these animal experiments. To date there has been no report of serious side-effects when erythromycin was administered to patients with various types of systemic infections, although mild gastrointestinal symptoms have been noted in some cases.[3] These symptoms, which include nausea, vomiting, diarrhea, or abdominal cramps, seem to be due to a direct action of the drug on gastrointestinal motility.

The laboratory work of McGuire and his associates,[1] Haight and Finland,[4] Heilman and his associates,[3a] and the laboratories of the pharmaceutical houses that produce this antibiotic indicates that erythromycin is a wide range antibiotic with particular activity against gram-positive organisms, whereas the coliform and enteric gram-negative bacilli are resistant. The list of sensitive organisms includes various types of Pneumococcus, groups A to G of Streptococcus hemolyticus, some strains of nonhemolytic streptococci, staphylococci, Corynebacterium diphtheriae, Clostridium tetani, Cl. perfringens, Cl. septicum, Bacillus anthracis, Listerella monocytogenes, Hemophilus pertussis, Pasteurella tularensis, Neisseria gonorrhoeae, and certain rickettsias and larger viruses. The list of resistant organisms includes Escherichia coli, Aerobacter aerogenes, Proteus vulgaris, Pseudomonas aeruginosa, and Salmonella typhosa.

The first clinical reports on the systemic administration of erythromycin for the treatment of various types of infections were those of Heilman and his associates,[3a] and Haight and Finland.[3b] They reported that it was particularly effective for the treatment of pneumococcic pneumonia and hemolytic streptococcic infections such as pharyngitis, tonsillitis, carbuncles, cellulitis, and erysipelas. These clinical results corresponded to the impressive in vitro effect of the antibiotic for the etiological agents of these diseases. It is of particular interest that strains of streptococci and staphylococci that were resistant to other antibiotics (penicillin and the broad spectrum antibiotics) were found to be as sensitive to erythromycin as the nonresistant strains.

The study here reported concerns the evaluation of erythromycin as a topical therapeutic agent. We have observed a series of 184 patients with various types of cutaneous bacterial infections, all of whom received local treatment with the antibiotic. We have had some experience with the oral administration of erythromycin in patients with extensive cutaneous bacterial infections, but this will not be included in this paper. The results of in vitro tests with erythromycin and other antibiotics of numerous strains of the two bacterial organisms (Micrococcus pyogenes var. aureus, and beta hemolytic streptococci) that are of particular importance in cutaneous bacterial infections will be reported, and an attempt will be made to correlate these data with clinical results.

METHOD OF TREATMENT

All but a few of our patients were treated with some type of ointment preparation, the exception being the use of compresses or soaks of an aqueous solution of 0.5 mg. of erythromycin per cubic centimeter of water. Because of our previous experience with the topical

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The powdered antibiotic for the preparation of ointments, the 0.5% erythromycin ointment in base 23 (Erythroguent), and the combination of 0.5% erythromycin and 0.5% neomycin sulfate ointment (Erythromycigluent) were supplied by Dr. Harold R. Reames, the Upjohn Company, Kalamazoo, Mich.; the 1% erythromycin ointment (Erythrocin ointment 1%) was supplied by Dr. George Berryman, the Abbott Laboratories, North Chicago, Ill. The neomycin lotion was also supplied by the Upjohn Company.

1. McGuire, J. M., and others: "Ilotycin," a New Antibiotic, Antibiotics and Chemother. **2**: 281-283 (June) 1952.

2. Brochure on erythromycin, the Upjohn Company, Kalamazoo, Mich.

3. (*a*) Heilman, F. R.; Herrell, W. E.; Wellman, W. E., and Geraci, J. E.: Some Laboratory and Clinical Observations on a New Antibiotic, Erythromycin ("Ilotycin"), Proc. Staff Meet., Mayo Clin. **27**: 285-304 (July 16) 1952. (*b*) Haight, T. H., and Finland, M.: Laboratory and Clinical Studies on Erythromycin, New England J. Med. **247**: 227-232 (Aug. 14) 1952.

4. (*a*) Haight, T. H., and Finland, M.: The Antibacterial Action of Erythromycin, Proc. Soc. Exper. Biol. & Med. **81**: 175-183 (Oct.) 1952. (*b*) Haight, T. H., and Finland, M.: Observations on Mode of Action of Erythromycin, ibid. **81**: 188-193 (Oct.) 1952. (*c*) Haight and Finland.[3b]

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application of other antibiotics, we decided to use a concentration of 5 mg. of the antibiotic per gram of ointment base, although a few patients were treated with 1% erythromycin ointment (10 mg. per gram in petrolatum). In 44 of these patients, a combination of 5 mg. of erythromycin and 5 mg. of neomycin sulfate per gram of ointment base was either the only local treatment or the effect of this combination was compared with the plain erythromycin ointment. Another variable that was introduced in the ointment used for some patients was the addition of moniliostatic agents (0.2 mg. of methylparaben-U. S. P., and 1.8 mg. of n-butyl *p*-hydroxybenzoate per gram of ointment base). The ointment bases that were used included (1) white petrolatum, (2) a wool fat-petrolatum base, (3) a cholesterol-petrolatum base, and (4) Aquaphor (a hydrophilic ointment containing hydroxyl animal fats). We did not use erythromycin in a water-miscible base because of the instability of the antibiotic under these circumstances.

The patients were instructed to apply the ointment either two, three, or four times daily. In some cases, the application of the ointment was followed by bandaging of the part (usually with Surgitube gauze), and in these patients the bandage was changed twice daily. Removal of crusts and other forms of local débridement were not emphasized, and the patients were not instructed to carry out cleansing of the affected parts; this routine was followed only because we attempted to avoid as many

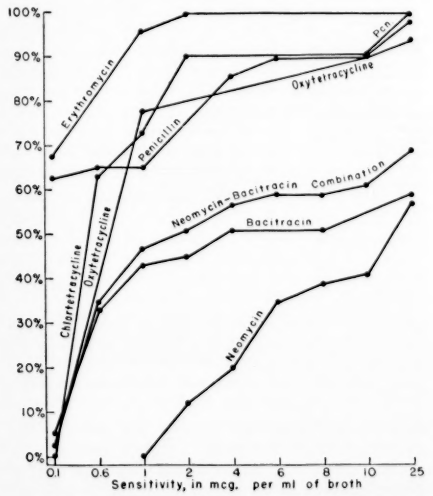

Fig. 1.—Results of in vitro sensitivity tests with various antibiotics of 60 strains of Micrococcus pyogenes var. aureus (hemolytic Staphylococcus aureus). All the strains were coagulase positive.

variable factors as possible. When possible, the erythromycin preparation was applied to the lesions on one affected site, and the plain ointment base to lesions at another site; the distribution pattern and other factors made it impossible to carry out this controlled experimental approach in the majority of patients. The fact that some of these patients had had previous ineffective topical and systemic therapy served as a control in other cases.

Bacterial cultures were done in almost all cases, and in many instances the cultures were repeated during and after the course of treatment. In vitro sensitivity tests to

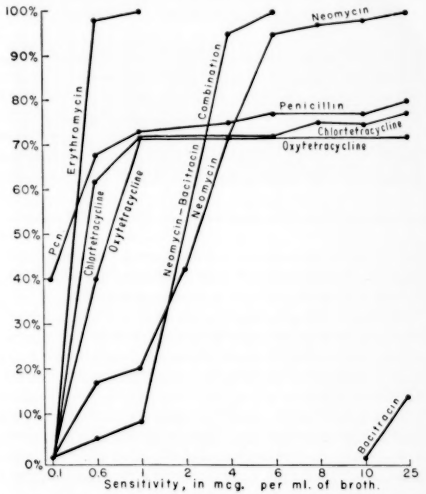

Fig. 2.—Results of in vitro sensitivity test with various antibiotics of 49 strains of Streptococcus pyogenes (beta hemolytic streptococci).

erythromycin, penicillin, chlortetracycline (aureomycin), oxytetracycline (Terramycin), neomycin, bacitracin, and the combination of equal parts of bacitracin and neomycin sulfate, with the standard multiple tube method, were done for 60 strains of M. pyogenes var. aureus (Staph. aureus) (fig. 1) and 49 strains of Strep. pyogenes (beta hemolytic streptococci) (fig. 2), hereafter referred to as hemolytic Staph. aureus and hemolytic streptococci. With this method the size of the inoculum is 1 by 10^6. All tests are read at the end of 24 hours. Tryptose phosphate broth was used for staphylococci, and horse meat infusion broth was used for streptococci.

RESULTS

Our results with topical erythromycin therapy are summarized in tables 1 and 2. We did not attempt to evaluate the comparative efficacy of the various types of ointment bases, although in general we noted no significant difference. Furthermore, our experience with the combination of erythromycin and neomycin as compared with erythromycin alone was not sufficient to be of statistical significance. We did not note a superior therapeutic effect when the concentration of erythromycin was increased to 1% (10 mg. per gram of ointment base) rather than 0.5%.

Erythromycin ointment and the combination of erythromycin and neomycin sulfate ointment in all types of ointment bases studied were very effective in almost

all of the 41 patients (fig. 3 and 4) with various types of primary cutaneous bacterial infections. We have not included exact data that pertain to the average number of days of treatment that were necessary to affect the clinical results, because to do so would involve the daily observation of each patient and that was not possible. However, in general, the patients with impetigo were cured within a period of from three to seven days. Those

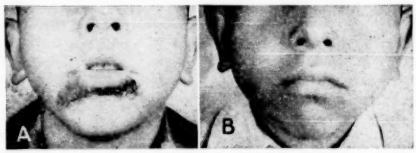

Fig. 3.—*A*, impetigo contagiosa before treatment with 0.5% erythromycin ointment applied three times daily for three days. *B*, after treatment.

with ecthyma were cured within a period of from 6 to 14 days. The one patient with pustular folliculitis who did not improve significantly was uncooperative.

As would be expected, the results in the treatment of the group of patients with various types of so-called secondary cutaneous bacterial infections, summarized in table 2, were more variable. It is necessary to emphasize that those patients whom we classified as "improved" had very satisfactory results in that the apparent bacterial infection factors was controlled completely insofar as this could be determined, but complete cure did not occur. Therefore, they were classified under the category of "improved" rather than "excellent."

It is obvious that numerous other predisposing and etiological factors must be considered in treatment of secondarily infected dermatitis of various types, otitis externa, perleche, nummular eczema, and ulcers. For example, one would not expect to effect a cure of atopic dermatitis by control of the secondary bacterial infection. We have the impression that local and systemic antibiotic therapy does not influence the course of kerion celsi significantly.

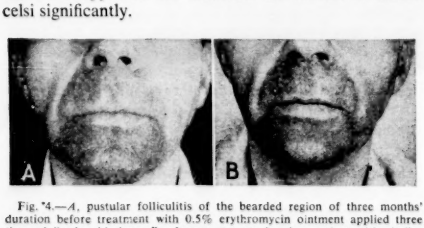

Fig. 4.—*A*, pustular folliculitis of the bearded region of three months' duration before treatment with 0.5% erythromycin ointment applied three times daily for 14 days. *B*, after treatment. Another patient with similar involvement did not have a satisfactory therapeutic result with erythromycin ointment.

It is well known that patients with nummular eczema do not tolerate greasy ointment vehicles, and it has been our experience that other antibiotic ointments are not particularly useful in the management of this condition. This must be kept in mind in interpreting the results with erythromycin ointment in this series of five patients.

It is difficult to evaluate the influence of any topical medicament in effecting the healing of removal sites. In some patients, especially those with removal sites on exposed surfaces, healing seems to proceed more promptly when no topical treatment is applied. If significant secondary bacterial infection occurs in a removal site incident to an electrocoagulation procedure, such as the treatment of an epithelioma, local antibiotic therapy may be very effective. In some cases erythromycin ointment seemed to be specific in its effect, but in other cases the application of an antibiotic in the form of a lotion effected more rapid healing of the removal site after the application of erythromycin ointment was discontinued.

TABLE 1.—*Results of Topical Treatment with Erythromycin of Primary Cutaneous Bacterial Infections*

Diagnosis	No. of Patients	Results				No. with Reaction to Treatment
		Excellent	Improved	Questionable	No Effect	
Impetigo contagiosa	13	12	1	0	0	0
Ecthyma	14	14	0	0	0	0
Folliculitis, pustular	8	5	2	1	0	0
Furunculosis	5	5	0	0	0	0
Paronychia	1	1	0	0	0	0
Total	41	37	3	1	0	0

TABLE 2.—*Results of Topical Treatment with Erythromycin of Secondary Cutaneous Bacterial Infections**

Diagnosis	No. of Patients	Results				No. with Reaction† to Treatment
		Excellent	Improved	Questionable	No Effect	
Impetiginized dermatitis ‡	33	18	10	1	4	0
Impetiginized eczematous dermatitis	38	7	12	6	13	2
Impetiginized atopic dermatitis	11	0	8	1	2	0
Impetiginized herpes simplex	2	2	0	0	0	0
Impetiginized cheilitis	1	1	0	0	0	0
Nummular eczema	5	0	0	1	4	1
Otitis externa	6	3	2	0	1	0
Removal sites	30	22	2	1	5	0
Ulcers	6	1	1	2	2	0
Kerion celsi	3	0	1	0	2	0
Folliculitis decalvans	1	1	0	0	0	0
Granuloma inguinale	1	0	0	0	1	0
Perleche	3	1	0	0	2	0
Achromia parasitica	3	0	2	0	1	0
Total	143	56	38	12	37	3

* In these patients, bacterial infection seemed to be an apparent complicating factor; in some patients with impetiginized eczematous dermatitis and otitis externa, bacterial infection was the possible primary etiological factor, and in many patients with impetiginized dermatitis and removal sites, the bacterial infection had delayed healing significantly.

† See the tabulation in the text.

‡ Secondarily infected contact dermatitis, superficial fungus infection, and others.

The rather high percentage of results that were classified as excellent (22 of 30 patients) must be interpreted with the reservation that this indicates only that healing occurred following the use of the erythromycin ointment; this does not mean necessarily that the treatment was responsible for more rapid healing of the lesions.

REACTIONS TO TREATMENT

Three patients had distinct, clear-cut exacerbations of their skin lesions following the application of erythromycin ointment. In each instance, the cause was traced to the erythromycin rather than to the ointment base. In two of these patients the erythromycin ointment was

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reapplied after the reaction had subsided, and the same sequence of events occurred. Patch tests to erythromycin ointment were positive in only one of these three patients (only two patients were tested). In the following tabulation we have summarized the other reactions (in addition to those due to erythromycin shown in table 2) that were noted in this series of patients. Both groups of patients treated with a neomycin-erythromycin combination had previously had no reaction to erythromycin ointment.

Erythromycin	3
Combination of neomycin-erythromycin (one patient with removal site and one with otitis externa)	2
Questionable reactions to neomycin-erythromycin ointment (eczematous dermatitis)	3
Ointment base containing lanolin (two patients with eczematous dermatitis and one with atopic dermatitis)	3
Apparent delayed healing of removal sites	2

RESULTS OF BACTERIAL CULTURES

The organisms that were isolated on bacterial culture in this series of patients were (1) M. pyogenes var. aureus (hemolytic Staph. aureus) in 45% of cases, (2) the combination of hemolytic Staph. aureus and Streptococci (beta hemolytic streptococci) in 28% of cases, (3) hemolytic streptococci (pure culture) in 8% of cases, (4) Staph. albus in 9% of cases, and (5) Pseudomonas, Proteus, A. aerogenes, or other gram-negative bacilli in 10% of cases.

RESULTS OF IN VITRO SENSITIVITY TESTS

In vitro tests were done for 60 strains of M. pyogenes var. aureus (hemolytic Staph. aureus) and 49 strains of Strep. pyogenes (beta hemolytic Streptococcus). All of these strains were tested to erythromycin and five other antibiotics as well as the combination of equal parts of bacitracin and neomycin. Our results are summarized in figures 1 and 2, which are self-explanatory. In addition, a few strains of Pseudomonas, Proteus, and Esch. coli were tested with erythromycin, and in all cases the sensitivity level was more than 50 mcg. per milliliter.

Analysis of these results indicates that for staphylococci the order of in vitro effectiveness of these antibiotics was erythromycin, neomycin-bacitracin combination, neomycin, chlortetracycline, oxytetracycline, and bacitracin (penicillin is not considered in this list because it is not recommended for topical application). For hemolytic streptococci the order of effectiveness was erythromycin, chlortetracycline, oxytetracycline, neomycin-bacitracin combination, bacitracin, and neomycin. It is interesting to note that, in the sensitivity tests done with penicillin, chlortetracycline, and oxytetracycline, there was very little difference in the percentage of sensitive strains through the range of concentration from 0.6 mcg. to 25 mcg. per milliliter; this was in striking contrast to the results that were recorded for neomycin and the combination of neomycin and bacitracin in that an increase of concentration from 2 mcg. to 6 mcg. per milliliter resulted in a very marked increase in the percentage of sensitive strains. This same phenomenon was noted in the case of beta hemolytic streptococci. In other words, with chlortetracycline, penicillin, and oxytetracycline, a given percentage of these strains of both staphylococci and streptococci tended to be very sensitive to the antibiotic or relatively resistant.

COMMENT

It is almost impossible to define the sensitivity of a given organism to an antibiotic when it is applied topically. One would assume that it is possible to maintain a very high concentration of the antibiotic at the site of involvement in contrast to the relatively low blood level with systemic administration of an antibiotic. In practice, however, the clinical results do not seem to follow this pattern. In most cases, it has been our experience that adequate control of the bacterial infection factor following topical application of the antibiotic may be expected if the sensitivity of the organism is of the order of magnitude of from 0.1 to 10 mcg. per milliliter; the clinical response seems to be more rapid and more predictable if the sensitivity level is not more than from 4 to 6 mcg. per milliliter. In contrast, it is our impression that the clinical results to be expected when the sensitivity level is higher than 10 mcg. are unpredictable and in general not satisfactory.

In previous papers [6] we have summarized our own experience and opinions as well as those of other investigators [7] in regard to the relative effectiveness of the various antibiotics that are available for the topical and the systemic treatment of cutaneous bacterial infections. Of the available antibiotics that are suitable for topical use, we prefer the combination of neomycin sulfate and bacitracin, oxytetracycline, chlortetracycline, and neomycin sulfate; polymyxin B is the local treatment of choice only for cutaneous infection due to Pseudomonas organisms.

The clinical results that we have summarized in tables 1 and 2 indicate that erythromycin is another effective antibiotic for the local treatment of cutaneous bacterial infections due to hemolytic Staph. aureus and beta hemolytic streptococci. The antibiotic is not effective for the gram-negative organisms, which seem to be of etiological importance in some cases; the addition of neomycin sulfate to the ointment results in a preparation that does have a gram-negative antibacterial spectrum. It appears to be at least as effective for streptococci as chlortetracycline, oxytetracycline, and the combination neomycin-bacitracin preparations and as effective for staphylococcic infections as neomycin sulfate. In a few patients with chronic impetiginized eczematous dermatitis, it was more effective in that the condition was cured or marked improvement effected after treatment with other antibiotics (both local and systemic) had failed.

We have the impression that erythromycin is slightly more irritant for denuded and eczematized skin than neomycin, bacitracin, chlortetracycline, and oxytetra-

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7. Miller, J. L.; Slatkin, M. H., and Johnson, B. A.: Evaluation of Bacitracin in Local Treatment of Pyogenic Infections, Arch. Dermat. & Syph. **60**: 106-120 (July) 1949. Sawicky, H. H.; Pascher, F.; Frank, L., and Rosenberg, B.: Therapeutic Assays of Skin and Cancer Unit of New York University Hospital: Aureomycin Hydrochloride Ointment, J. Invest. Dermat. **15**: 339-341 (Oct.) 1950. Kile, R. L.; Rockwell, E. M., and Schwarz, J.: Use of Neomycin in Dermatology, J. A. M. A. **148**: 339-343 (Feb. 2) 1952. Wright, C. S., and Tschan, D. N.: Local Oxytetracycline ("Terramycin") Therapy of Skin Infections, A. M. A. Arch. Dermat. & Syph. **67**: 125-128 (Feb.) 1953.

cycline. We do not have evidence at this time, however, that the antibiotic has a higher sensitizing potential than the other antibiotics that are recommended for topical use. Additional experience must be accumulated before the semipermanent or final place of erythromycin in our therapeutic armamentarium for the local treatment of cutaneous bacterial infections is established.

Finally, if a sensitizing antibiotic such as penicillin is not considered, there is close correlation between the in vitro sensitivity tests and the clinical results. In this respect erythromycin shows great promise provided an increased percentage of irritant and/or sensitization reactions does not interfere with its therapeutic effect. However, the possibility of subsequent development of resistant strains of staphylococci and streptococci must be considered.

SUMMARY AND CONCLUSIONS

Our experience with the topical use of erythromycin in the treatment of cutaneous bacterial infections is reported; a total of 184 patients is included in this series. The majority of these patients were treated with a 0.5% ointment. A combination of neomycin-erythromycin ointment was used in some cases. It appears that erythromycin is a very effective topical therapeutic agent for staphylococcic and streptococcic primary cutaneous infections; the results in secondary bacterial infections were variable. Results of in vitro tests for 60 strains of hemolytic Staphylococcus aureus and 49 strains of beta hemolytic streptococci are reported; drugs used in this in vitro study included erythromycin, chlortetracycline (aureomycin), oxytetracycline (Terramycin), penicillin, neomycin, bacitracin, and a combination of equal parts of bacitracin and neomycin sulfate. Three patients had an apparent sensitivity or irritant reaction to erythromycin, and two additional patients had a similar reaction following application of the neomycin-erythromycin combination ointment. One of the ointment bases (lanolin) was not tolerated in three other patients. It is possible that erythromycin is not as well tolerated by denuded and eczematized skin as certain other antibiotics.

SEX AND AGE IN MYASTHENIA GRAVIS AS CRITICAL FACTORS IN INCIDENCE AND REMISSION

Robert S. Schwab, M.D.
and
Charlotte C. Leland, A.B., Boston

Since the communication on removal of the thymus as treatment for myasthenia gravis was presented by Blalock [1] in 1941, there have been a number of other reports on this procedure as a therapy in myasthenia gravis. Some of these have been enthusiastic as to the benefits achieved by removal of thymic tissue, particularly when it was not associated with tumor, in producing complete or partial remission in this disease. Geoffrey Keynes has reported the largest series of such operations, nearly 200. The first 100 of his patients were studied in considerable detail by Ross,[2] who reported that the operation benefited 86 patients. There was statistical evidence that the sooner the operation was done after the onset of the disease the more favorable the result. On the other hand, Eaton and Clagett [3] reported little statistical difference in remission rate between 70 patients treated by this operation and their control group of patients that had not been treated surgically.

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1. Blalock, A.; Harvey, A. M.; Ford, F. R., and Lilienthal, J. L., Jr.: Treatment of Myasthenia Gravis by Removal of Thymus Gland: Preliminary Report, J. A. M. A. **117**: 1529 (Nov. 1) 1941.

2. Ross, R. T.: Thymectomy in Treatment of Myasthenia Gravis, Lancet **1**: 785, 1952.

3. Eaton, L. M., and Clagett, O. T.: Thymectomy in Treatment of Myasthenia Gravis, Results in 72 Cases Compared with 142 Control Cases, J. A. M. A. **142**: 963 (April 1) 1950.

4. Schwab, R. S., and Passouant, P.: Les indications de la thymectomie au cours de la myasthénie, Presse méd. **60**: 1501, 1952.

5. Eaton, L. M., and Bastron, J. A.: Thymus Gland and Its Relationship to Diseases of Nervous System, in Metabolic and Toxic Diseases of the Nervous System, A. Res. Nerv. & Ment. Dis., Proc., vol. 32, to be published, 1953.

Schwab and Passouant [4] reported on 50 patients with thymectomy, in whom the remission findings were correlated with sex and age. The most favorable results were found in the young female group rather than in males. Eaton [5] reported a reevaluation of the results of thymectomy in his series, and indicated that there was new evidence that made him feel that the operation produced a greater percentage of remissions than in the control series, but he was not quite satisfied with the statistical analysis of this material. There still is, therefore, some question as to the precise value of thymectomy in myasthenia gravis in spite of study of adequate numbers of patients subjected to the procedure and comparison of these results with a control series.

Since there was a difference in response to the operation in females and males, we plotted the onset of the disease according to decades in the two sexes in a total group of 367 patients on whom we had accurate information about the date of onset (fig. 1). This showed a significant and surprising difference between males and females. The disease developed in 62% of the 202 females before the age of 31. In contrast to this early beginning in the females, in the 167 males the onset occurred before the age of 30 in only 27%. For females the mode (21%) onset age was 21 to 25 years, whereas for males the mode (30%) onset age was 61 and over.

The significance of this sex difference in onset is at once apparent in the various series of thymectomy cases reported in the literature, and in all of them there are two or three times as many females as males. This would be the obvious result of random selection of the surgical cases, since the most favorable subject for a serious op-

eration such as thymectomy would be the younger patients. In our group of 78 patients, 53 were females and 25 were males.

In analyzing our data, we used controls that matched the thymectomy patients by sex, age of onset (within five years), severity of disease, and presence or absence of thymoma. These factors had all been found important in determining the good effects of thymectomy. The 78 controls were selected from a group of 250 myasthenia gravis patients. The influence of these variables was then compared. Patients in both groups were classified as to the presence of a remission as follows:

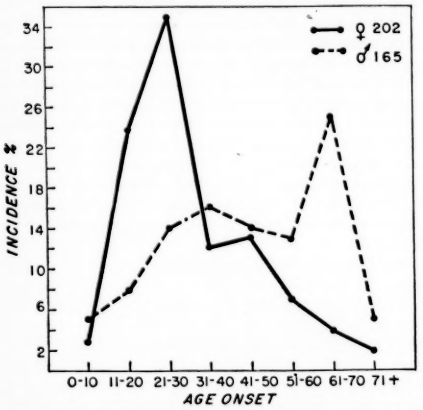

Fig. 1.—The distribution by decades of the onset of myasthenia in 367 patients.

A. This group had a complete remission. They no longer required any medication and had no symptoms.

B. This group was significantly and objectively improved, took less medicament, and had fewer symptoms. Medical referees would all agree as to the presence of improvement.

C. In this group were included patients with various degrees of slight to moderate improvement, which was subjective oftener than objective, difficult to evaluate quantitatively, and would not convince skeptical referees.

D. This group consisted of patients whose symptoms were unchanged or worse.

E. This group included the patients who died. The operative deaths and deaths from myasthenia were grouped together.

RESULTS

There was no significant mathematical difference in remission rates in relation to age or sex in the patients who had thymomas that were removed. In male patients subjected to thymectomy there was an A or B remission rate of 24% compared to a remission rate of 56% in males who did not have a thymectomy. Males subjected to thymectomy had the lowest remission rate and the highest mortality rate (table 1).

The A or B remission rate of females subjected to thymectomy was 63% contrasted with an AB remission rate of only 34% in those not subjected to surgery. This difference is statistically valid at the 1% level when tested by the Chi square formula. The mortality rate is correspondingly different for the two groups, the controls having nearly twice the mortality rate of the females subjected to thymectomy (28% vs. 15%). Figure 2 shows this in graphic form. In 44 females without thymomas, the A or B remission rate was 68%. These figures are conservative, as exclusion of thymoma cases raises the

TABLE 1.—*End Results* of Myasthenia Gravis With and Without Thymectomy*

Females

With Thymectomy	No. of Patients		%	Control	No. of Patients		%
A.	11	33	63	A.	7	18	34
B.	22			B.	11		
C.	4	12	22	C.	13	20	38
D.	8			D.	7		
E.	8	8	15	E.	15	15	28
Total		53	100	Total		53	100

Males

With Thymectomy	No. of Patients		%	Control	No. of Patients		%
A.	2	6	24	A.	4	14	56
B.	4			B.	10		
C.	5	11	44	C.	4	6	24
D.	6			D.	2		
E.	8	8	32	E.	5	5	20
Total		25	100	Total		25	100

* AB vs total in female groups significant at 1% level.
AB vs total in male groups significant at 5% level.
AB vs E (deaths) in both groups significant at 5% level.
E vs total is not significant in both groups.

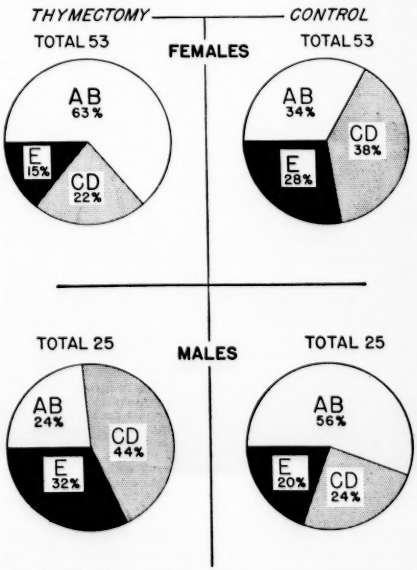

Fig. 2.—An analysis of the effect of thymectomy in 78 patients (53 females and 25 males) compared with a similar group of controls. Note the better remission rate and lower mortality in the females subjected to thymectomy as compared to the controls. The reverse was true of the males.

AB remission rate of the females subjected to thymectomy and lowers the mortality rate. We avoid comparison of the groups that did not have thymomas, as it is possible that some controls had thymomas that were not detected on chest roentgenograms.

It was suggested that we determine the remission rates at some specific time after thymectomy to see if they differ significantly from the end result figures. In 44 females without thymomas, for example, 59% could be classified

TABLE 2.—*Relation of AB Remission Rate to Total Known Duration of Myasthenia in Patients Subjected to Thymectomy and Controls*

	Females						Males					
	With Thymectomy			Control			With Thymectomy			Control		
Duration, Yr.	No. of Patients	No. with AB Remission	%	No. of Patients	No. with AB Remission	%	No. of Patients	No. with AB Remission	%	No. of Patients	No. with AB Remission	%
0-3	12	7	58	21	8	38	8	2	25	7	3	42
4-7	25	17	68	19	3	16	5	1	20	5	3	60
8+	16	9	51	13	7	54	12	3	25	13	8	62

in groups A or B within one year of the operation. There is no significant difference between the rates found within one year and those shown in table 1.

A study of the duration of illness from the onset to the time thymectomy was done showed that a duration of none to four years is apparently beneficial for females (not significant to 5% level) but not for males. These groups were analyzed as to age of onset to see whether more young patients were included in the short duration group, thus causing the increased benefit. This was not so, since the group of females with shorter duration was complicated by more thymomas and older patients. This

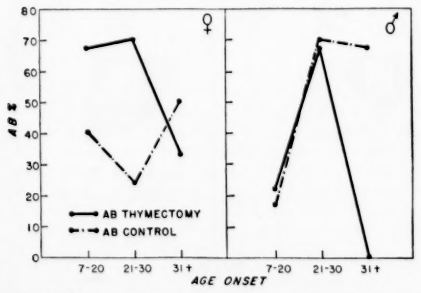

Fig. 3.—The rate of AB remissions in relation to age of onset in the two sexes, in patients subjected to thymectomy, and in control groups. Note that there is no significant difference between the second and third decades in the group subjected to thymectomy, but the remission rate is worse in the controls between the ages of 20 and 30. There is a sharp drop in the remission rate in females over 30 who have been subjected to thymectomy. Before the age of 30 there is no difference in the remission rate of males subjected to thymectomy and the controls, but there is a sharp decrease in the benefits of the operation in males over 30.

agrees with the conclusion of Keynes that early intervention increases the remission rate. One should note that more of his patients were females in a ratio of 3: 1, and we believe that early intervention increases the remission rate only for the females. Table 2 illustrates this finding. Female thymectomy patients who have had their disease over seven years had slightly less improvement than their controls. This figure suggests that a female having myasthenia gravis for that length of time would be better off without thymectomy. Male controls tended to improve with the passage of time. This natural tendency to improve was offset in the thymectomy cases.

The exclusion of thymoma cases raises the AB remission rates (except for males) and lowers the death rate. The thymoma patients of both sexes who did well had mild myasthenia. Male patients with or without thymomas who were subjected to thymectomy had the same low (24%) rate of AB remissions, although the mortality rate for all males (32%) is nearly double that of the group without thymomas (18%). Thymomas were present in 29% of males in whom the onset was before age 31 and in 36% of those over 30. The radical drop in AB remissions for males over 30 (statistically significant at the 1% level) is not due to the presence of thymomas, nor is there an increased proportion of severe cases in the older group.

Of the female thymectomy patients, only 5% of those under 31 and 78% of the older patients (a total of nine) had thymomas. The high proportion of thymomas in older females probably explains their poorer result. Thymectomy in patients with thymoma lowered the remission rate for females, did not alter it for males, and raised the death rate for both. Thymectomy is of uncertain value as a therapeutic measure in myasthenia gravis in all patients with demonstrable tumors such as thymomas and in all males.

The method of selection of patients for thymectomy depended partly on chance, economic reasons, and random persuasion in different periods by a number of different physicians, with a large number of variables. There has been, however, a trend toward selection of younger patients. In the period 1938-1945 in 44% of patients of both sexes combined the onset was after 30, whereas for 1946-1953 only 21% were of the older group. There has been a change in the proportion of males to females operated upon from 12 of 17 (71%) for the earlier period to 13 of 48 (21%) for the later period. Fewer patients with thymomas were selected in the later period, especially among males, where the proportion dropped from 42% to 23%. The decrease in patients with thymomas and in older patients and the increase in females are factors in the improvement of the results of thymectomies over the years.

The value of thymectomy in the females under 30 is compared to spontaneous improvement in the control group in figure 3. In the male group there is no difference in results in the surgical and control groups of patients under 30 years of age. In males over 30, the operation seems contraindicated, as shown in this figure.

COMMENT

In spite of the positive statistical correlation in these groups of cases, particularly in the group of females subjected to surgery as opposed to the controls, some investigators feel that the benefit of this chest operation in myasthenia patients may be due to the stress effect of the procedure. One can dismiss this, because myasthenia

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patients who have had major operations such as hysterectomy, or those who have suffered major fractures from accidents, emotional stresses, severe financial catastrophe, or death of loved ones, show a contrary effect under the stress of such trauma. Universally they show an increase in myasthenia symptoms and require more medication. They return to their previous condition only after a lapse of time. Of 30 patients who encountered such stressful situations, 28 showed a temporary increase in their disease.

Some clinicians are skeptical that there is any relation at all between myasthenia and the thymus gland. According to our figures, 17 (22%) of 78 patients subjected to thymectomy had thymomas. In Rowland's [6] series of 35 cases of death due to myasthenia, there was a 31% incidence of thymomas. The incidence of thymomas in ordinary postmortem examinations (in cases without myasthenia) is less than 1/10 of 1%. In our thymectomy cases, 60% of patients who did not have thymomas had abnormal thymic tissue in the sense that there was hyperplasia or presence of germinal center formations. The relationship seems indisputable. In view of the poor results of thymectomy in patients with thymomas and in male patients irregardless of pathology, it is likely that the causal agent is not the thymus itself but another endocrine disturbance that may cause both the thymic abnormalities and the myasthenia.

In our series of patients we feel that we have sufficient data to warrant the conclusion that the operation is indicated in younger females. In the 25 males who have been subjected to this procedure, our statistical consultants feel that a dogmatic conclusion of contraindication is not justified. They did not recommend, however, that additional males be operated on in order to increase the size of the group.

The seriousness of this disease is shown by the relatively high mortality rate. It is worth emphasizing that the females subjected to thymectomy have a decreased mortality rate (15%) as compared to their controls (28%). This includes the operative mortality, which was 7.5%. The operative mortality for males was 24%. An examination of the operative mortality rate for both sexes reveals that, prior to 1946, 5 of 17 patients died (29%). From 1946 through 1952, 5 out of 61 patients died (8%). Our data suggest that the young female patient has twice the chance of survival with thymectomy, and this better chance of survival is greatly increased owing to the experience of the surgical team, anesthesia personnel, and neurological indoctrination of the house staff.

SUMMARY AND CONCLUSIONS

The progress of 78 patients who have undergone thymectomy is analyzed and compared to a similar group who have not had surgery. The patients of all ages and both sexes who had thymomas demonstrable by either gross or microscopic examination derived no evident improvement in their myasthenia from the operation. Males received no evident benefit from the operation. Thymectomy appears to be contraindicated in males in whom the onset of the disease was after 30.

In females without thymomas, thymectomy appears definitely indicated. The incidence of unquestionable improvement in all 53 females who were subjected to thymectomy was 63% as opposed to 34% in the controls. The mortality rate, including operative deaths, was 15% for female thymectomy patients and 28% for their controls. More data indicate that the disease is twice as common in young females as in young males and twice as common in older males as in females.

6. Rowland, L. P.: Fatalities in Myasthenia Gravis, Tr. Am. Neurol. A., 1953, to be published.

SPECIAL ARTICLE

A HISTORICAL REVIEW OF MYASTHENIA GRAVIS FROM 1672 TO 1900

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Although myasthenia gravis was not described with any pretense of completeness as a clinical entity until the last quarter of the 19th century, a reference by Thomas Willis, an astute 17th century English clinician, indicates that Willis knew of the disease and recognized the chief symptom of asthenia of the voluntary muscles, with recovery after rest. The description of the weakness in his patient (1672),[1] first noticed by Guthrie (1903),[2] occurs in his book on the physiology and pathology of disease, with illustrative cases, "De anima brutorum," published in two separate editions the same year in Oxford and in London.

An English translation of "De anima brutorum" was made by S. Pordage in 1683 and published as "Two Discourses Concerning the Soul of Brutes" in "Dr. Willis's Practice of Physick" (London, 1684).[3] The significant part is as follows:

> There follows another kind of this Disease [i. e. the *Palsie*] depending upon the want and fewness of Spirits, in which, although motion be not deficient in any part or member wholly, yet it is not performed by any but weakly and depravedly only. For though the distemper'd are free from want of motion, they are not able however to move their members strongly, or to bear any weight; moreover, in every motive endeavour, they labour with a trembling of their limbs, which is only a defect of debility, and of a broken strength in the motive power. For when strength is wanting for the lifting up of any member firmly, and at one essay or endeavour, Nature flagging, acts with a more often repeated tryal or endeavour, and so the part being in motion is compelled as it were to shake and tremble . . . (p. 166).
>
> Not only *Scorbutical* persons, but also many others, hardly and long growing well from some *Chronical* Disease, are distemper'd with Members very much loosened from their due vigor and strength, and with a languishing of their Limbs; that though they are well in their stomach, and have a good and laudable Pulse and Urine, yet they are as if they were enervated, and cannot stand upright, and dare scarce enter upon local motions, or if they do, cannot perform them long: yea, some without any notable sickness, are for a long time fixed in their Bed, as if they were every day about to dye; whilst they lye undisturbed, talk with their Friends, and are

1. Willis, T.: De anima brutorum, Oxford, Theatro Sheldoniano, 1672, pp. 404-406.

2. Guthrie, L. G.: Myasthenia Gravis in the Seventeenth Century, Lancet **1**:330, 1903.

3. Willis, T.: Two Discourses Concerning the Soul of Brutes, translated by S. Pordage, London, 1683.

chearful, but they will not, nor dare not move or walk; yea they shun all motion, as a most horrid thing. Without doubt in these, although the Animal Spirits do after a manner actuate and irradiate the whole nervous Stock, yet their numbers are so small, and in so few heaps, that when as many spirits ought to be heaped together somewhere in it for motion, there is great danger left presently in the neighbouring parts, their continuity should be broken. Wherefore, when the spirits inhabiting the Brain, are conscious of the debility of others disposed in the Members, they themselves refuse local motions, for that it would be too difficult a task to impose on their companions; wherefore, the sick are scarce brought by any persuasion, to try whether they can go or not; Nevertheless, those labouring with a want of Spirits, who will exercise local motions, as well as they can, in the morning are able to walk firmly, to fling about their Arms hither and thither, or to take up any heavy thing; before noon the stock of the Spirits being spent, which had flowed into the Muscles, they are scarce able to move Hand or Foot. At this time I have under my charge a prudent and an honest Woman, who for many years hath been obnoxious to this sort of spurious *Palsie*, not only in her Members, but also in her tongue; she for some time can speak freely and readily enough, but after she has spoke long, or hastily, or eagerly, she is not able to speak a word, but becomes as mute as a Fish, nor can she recover the use of her voice under an hour or two (p. 167).

Thus Willis noted that his patients developed general, although partial, paralysis, that they were "not able however to move their members strongly, or to bear any weight," and that they "dare scarce enter upon local motions, or if they do, cannot perform them long." Some kept to their beds, neither wishing nor daring to be raised up or to walk about. In spite of the paralysis, his patients discoursed with their friends and were cheerful. Willis was particularly impressed by the strength shown by his patients in the morning. They were able to walk, move their arms, and lift a weight with strength; "before noon," however, "the stock of the Spirits being spent, which had flowed into the Muscles, they are scarce able to move Hand or Foot." The dysarthria of one patient, "a prudent and an honest Woman," was described in some detail by Willis. The disease had lasted for "many years" and was evident in the palsy not only of her limbs but also of her tongue. For some time she spoke "freely and readily enough," but after long, hasty, or laborious speaking she became "as mute as a Fish," only recovering her voice after an hour or two. There can be little doubt, therefore, that Willis, in the latter quarter of the 17th century, recognized the disease and described its principal symptoms.

Nearly 200 years were to pass, however, before myasthenia gravis was again referred to in the medical writings. The next recorded observation also was made by an English physician. Samuel Wilks (1877),[4] one of the physicians to Guy's Hospital, London, who, in describing some cases of bulbar paralysis and other neurological syndromes, described one patient with symptoms slightly suggestive of those seen in cases of myasthenia gravis. A girl could scarcely walk and had slight strabismus. No further change occurred in the first month; action and speech were slow and deliberate. At the end of this period she developed rapidly the additional symptoms of dysarthria and dysphagia. Unable to cough, she died of acute respiratory paralysis. The clinical record, as published, is so incomplete as to make the diagnosis difficult. Missing is the essential feature of myasthenia gravis, already noted by Willis, namely, recovery of muscular power after rest.

The report by Wilks, however, is important because the medulla oblongata was examined post mortem and no pathological signs of disease were found. "It appeared," wrote Wilks, "quite healthy to the naked eye, and the microscope discovered no manifest change in the tissue." This finding was strikingly different from the observations in cases of bulbar palsy, where cell degeneration was recognized by Wilks and his associates at Guy's as early as 1877.

Wilks' vague notation of 1877 passed almost unnoticed, as had the better account of Willis' patient, 200 years before. A more important presentation is that by Erb (1879),[5] who may be regarded as the first physician to write a reasonably full account of the syndrome. His paper was read May 18, 1878, although it was not printed until the next year. Two of his three patients were seen in Friedreich's clinic in Heidelberg, where Erb was serving at the time as a physician.

Wilhelm Heinrich Erb, aged 38 in 1878, and long interested in muscular disorders, had first used the galvanic and faradic currents for electrodiagnosis in 1868 and had described the form of brachial palsy that goes by his name in 1877. In 1878, his *Handbuch* in two volumes was in the course of publication.

Erb's first patient with myasthenia gravis, a man of 55, was seen in 1868, 11 years prior to the publication of his case record. The patient's illness had developed over a period of four months, the principal symptoms being bilateral ptosis, neck weakness, and dysphagia. Some atrophy was noted in the neck muscles, and the response to faradism in the trapezii, masseters, and splenii was diminished. In six months, with galvanism, decided improvement was noted. The patient, Georg Fuss, a day laborer, is worthy of notice, as he must have been one of the first patients examined and treated by electricity under Erb's care. When a remission occurred, it was natural for Erb to attribute the improvement to the galvanism. The patient was not followed beyond 1868.

A second patient from Friedreich's clinic was Magdalene Meisel, a peasant of 30 years of age, who was first seen on Oct. 17, 1870. Her early symptoms were diplopia and ptosis, dysphagia, and general weakness. During the next year there were frequent fluctuations in the severity of her disease. At one time she was nearly normal; later her speech became nasal, with marked general fatigue. After a period of recovery she died suddenly at night, in March, 1872. There was no postmortem examination. This is the first case in which there is a record of remissions and relapses. There is no mention of recovery after rest. Death occurred suddenly, as in Wilks' case.

Erb's third patient, August Thal, a merchant, aged 47, was first seen on July 11, 1871. For a year the patient had noticed weakness of his neck muscles. Later there was general weakness and he could not hold his head up. Bilateral ptosis was next observed, then weakness of the facial muscles. No improvement was noted after galvanism; the patient was followed only a month or two.

4. Wilks, S.: On Cerebritis, Hysteria, and Bulbar Paralysis, as Illustrative of Arrest of Function of the Cerebrospinal Centres, Guy's Hosp. Rep. **22**:7-55, 1877.

5. Erb, W.: Zur Casuistik der bulbären Lähmungen. (3) Ueber einen neuen, wahrscheinlich bulbären Symptomencomplex, Arch. Psychiat. **9**: 336-350, 1879.

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All three cases described by Erb appear, 74 years later, to be examples of myasthenia gravis. The case of Magdalene Meisel is the most characteristic, and the progress of her disease to death is a story often repeated in the literature in subsequent years. The other reports, while not so definite and lacking the length of observation needed to make an accurate diagnosis, nevertheless describe cases clearly enough that they may be classified as cases of types of myasthenia gravis.

Erb's paper is, therefore, incomplete. It is of value, however, for Erb first brought out clearly some of the chief symptoms of myasthenia gravis, particularly the distribution of the paralysis in the muscles supplied by the bulbar nuclei, the progress by remission and relapse, the sudden death, and the frequency of ptosis as the leading sign of the disease. He mentions other symptoms, however, not commonly found, such as hyperacusis in the first and second case, and headache, vertigo, and sharp pains in some of the others. In spite of the inadequacy of his descriptions, from the present point of view, it must be realized that these three patients were taken from a large number of patients with bulbar paralysis, certainly an ill-defined group in 1879, and considered to have a new symptom complex. The syndrome was not, however, given a definite name. With only brief histories and periods of observation and without postmortem studies, Erb saw something unusual about these three patients and had the genius to visualize a previously undescribed, as far as he was concerned, disease. Erb might rightly be considered the first physician to bring myasthenia gravis to the attention of the medical world. He published his paper, moreover, in a standard medical journal, which was, although only nine years old, devoted exclusively to psychiatry and neurology, where it was most likely to be seen and evaluated by others competent to judge its worth.

The first to do so was Eisenlohr (1887),[6] a physician from Hamburg, who added another case report eight years later. The patient, a girl, aged 18, was seen in the summer of 1886. His account is chiefly notable for his observation of variations in the patient's symptoms in the course of a single day, a point not previously mentioned by others. Chief emphasis was placed by Eisenlohr on the external ophthalmoplegia, which was accompanied by attacks of migraine, dating back to early childhood. The terminal manifestations of diaphragmatic paralysis, with no abnormalities found on postmortem examination, however, lead me to believe that a diagnosis of myasthenia gravis was justified. Death, in females at about this age, is one of the most characteristic features of the disease, as will be illustrated frequently in later reports.

Oppenheim (1887), an assistant in Westphal's clinic at the Charité in Berlin, reported still another case. While Oppenheim was the first to notice Wilks' case of 10 years before and quotes it in full, he does not mention for some reason the three cases described by Erb in 1879. Oppenheim was particularly interested in the differential diagnosis between hysteria and myasthenia gravis and noted that Wilks' house physician was inclined at first toward a diagnosis of hysteria in the London case. His patient, Pauline Jahnke, a 29-year-old maidservant, was observed for over a year. There was marked variation in the severity of her symptoms; she died in a dyspneic attack. The postmortem examination revealed no abnormalities.

The case reported by Shaw (1890),[7] although a careful study of the pons and medulla post mortem failed to show any signs of structural disease, is important historically because of the observation, first made by Willis, that the patient's "symptoms were but slight in the morning, but became more evident as the day advanced." This fact had long been unnoticed until revived by Shaw. The patient, a 37-year-old baker, had symptoms for only six months before death. He showed the usual dysarthria, dysphagia, diplopia, and difficulty in mastication and expectoration. Shaw notes particularly the "copious secretion of frothy mucus" and gives a vivid account of the terminal respiratory paralysis and failure of artificial respiration, reported for the first time in the treatment of myasthenia gravis.

The striking changes in the eye muscles were naturally one of the first symptoms to attract attention. Bernhardt (1890) made particular note of this. His patient, a joiner, aged 44, first noticed diplopia in August, 1866. By November there was double ptosis and difficulty in mastication. In February, 1877, he was well, and his remission lasted until 1890, the longest recorded up to that time. Six months later, however, neck weakness, dysarthria, and general weakness developed, with dyspnea, only to be followed by a brief period of improvement. The patient died suddenly before the year was out; there was no autopsy. The reporting of a 3 year remission, coming on 10 years after the onset of the disease, was the chief addition by Bernhardt to our knowledge.

An American student, Hermann Hoppe (1892),[8] working in Oppenheim's clinic and laboratory in Berlin, reported a fully studied case in 1892, with no abnormal findings at postmortem examination. Hoppe's patient, a blacksmith, aged 40, was observed for over a year with symptoms of bilateral ptosis, dysarthria, and dysphagia. There was weakness of both facial muscles, as well as those of mastication, the abductors and adductors of the vocal cords, and the extremities. Electrical reactions were normal, and there was no atrophy. The postmortem examination of the nervous system was more complete than in any previously described case; no lesions were found. Hoppe compared his case in detail with those of Wilks, Oppenheim, and Eisenlohr. His report contains the most comprehensive review of the disease up to 1892.

In a report on three cases of bulbar paralysis by Remak (1892), the second case is highly suggestive of myasthenia gravis, in spite of the fact that the girl was only 12 years of age. She suffered from influenza in February, 1890, and noticed facial weakness and dysarthria the following July. By September, she had dysphagia, nasal speech, and weakness of the tongue and lips. Some improvement followed, but she had difficulty in expectoration and attacks of dyspnea. Weakness of the arm was next noted. Death occurred from respiratory

6. Eisenlohr, C.: Ein Fall von Ophthalmoplegia externa progressiva und finaler Bulbärparalyse mit negativem Sectionsbefund, Neurol. Centralbl. **6**: 337-341, 361-365, 389-390, 1887.

7. Shaw, L. E.: A Case of Bulbar Paralysis Without Structural Changes in the Medulla, Brain **13**: 96-99, 1890.

8. Hoppe, H. H.: Ein Beitrag zur Kenntniss der Bulbärparalyse, Berl. klin. Wchnschr. **29**: 332-336, 1892.

paralysis in November. There was no postmortem examination. The chief interest in the case historically lies in the age of the patient, one of the youngest on record.

Dreschfeld (1893), of Manchester, England, described another case in great detail under the title of "Polioencephalomyelitis Without Any Anatomical Lesions." His report is the first emphasizing the long history of symptoms, characteristic of myasthenia gravis. Double ptosis at the age of 21 was followed, after six months, by a remission lasting five years. Five years later the patient suffered a second attack, which continued intermittently for 10 years. She died at the age of 36 of respiratory paralysis. An extensive postmortem examination failed to disclose any lesions in the nervous system. For 10 years, between the second and third attack, she was able to work as a dressmaker and in the bakehouse of an almshouse. She ate slowly, with frequent rest periods, supporting her jaw with her hand. There was also weakness of her shoulders. During the long period only the eye symptoms improved. In spite of the title of his report, Dreschfeld compares his case with those reported by Hoppe, Wilks, Eisenlohr, and others.

With a score or more cases reported by 1893, some with negative examinations of the pons and medulla, Goldflam (1893),[9] added greatly to our knowledge of the disease and his name is rightfully coupled with that of Erb in the eponym the Erb-Goldflam symptom complex. He not only added three important case reports to the literature but also analyzed the symptoms in a manner superior to any writer before him. He noted the early bulbar symptoms, which often come on in a few weeks or months after the onset, the facial weakness, and the involvement of the trunk and neck muscles. The rapid exhaustion of all muscles was particularly emphasized. He was not unmindful of remissions and exacerbations, particularly those occurring in a period of 24 hours or less. All three of his patients were worse in the evening. To differentiate his cases from bulbar paralysis as described by Duchenne, Goldflam pointed out the lack of atrophy of the muscles affected, the absence of fibrillation, the normal electrical responses, the presence of sphincter control, the normal or lively reflexes with reflex exhaustion after continuous stimulation, and the normal palatal reflex. Some of these points had been noted before, but Goldflam synthesized the whole picture and made clear the differential diagnosis between myasthenia gravis and bulbar palsy. Goldflam, moreover, stressed the attacks of dyspnea and, although none of his patients died under his observation, he nearly had a fatality as the result of the examination of the larynx of one of them. Finally, he noted the weakness of the muscles supplied by the fifth cranial nerve in myasthenia gravis, a muscle group rarely, if ever, paralysed in bulbar palsy. Entirely familiar with the previous literature, Goldflam realized that his three cases were examples of a benign type of the disease.

Goldflam, in his summary, established the following points: The disease often occurs in early life. The sexes are about equally affected. Myasthenia gravis is primarily a disease of the motor system, with only occasional pains or paresthesias; chewing, swallowing and eye movements are most affected at first, followed by involvement of the trunk and extremities. The disease rarely has its onset in the arms or legs. The muscular involvement is usually symmetrical. The muscles supplied by the facial nerve are always involved, mostly the middle and lower branches; the muscles of mastication and those of the neck are next commonly affected. Stimulation results in rapid weakness. Most patients are worse in the afternoon. Twenty or 30 movements often bring the muscle response to zero. Daily remissions and relapses occur, but remissions may last as long as four years. The knee jerk may be exhausted by stimulation. Death may occur very suddenly. All of Goldflam's observations are valid today; in fact, little has been added to the clinical description of the disease since his time. His paper in many ways is the most important ever written in the history of the disease.

After Goldflam's paper, other cases were soon reported. Suckling (1893) observed two nonfatal cases in young women; Wernicke (1893) described the now somewhat recognized syndrome in a young woman who died suddenly of asphyxia. Examination of the nervous system post mortem revealed no abnormalities except some vascular dilatation and recent hemorrhages. A similar case, with death from sudden choking, was reported by Mayer (1894). Wernicke's observation on the thymus was not to be made until 10 years later.

Jolly (1895),[10] who first gave the name myasthenia gravis pseudoparalytica to the disease, published reports of two cases. A preliminary report of the first case was given in 1891, but both cases were described in detail in 1895. The first patient was a boy of 15, with many symptoms of eight months' duration. When his muscles were stimulated repeatedly with faradism, a reaction of asthenia was promptly demonstrated. This, the "myasthenic reaction," was recorded in tracings. The patient died suddenly while eating, with a piece of food sticking in his throat. No abnormal changes were found in either the nervous system or in the muscles.

Jolly's second patient was also a boy, aged 14, who had had symptoms for over a year, beginning with ptosis. Subsequently, there was great weakness in his arms, legs, neck, and muscles of mastication. The speech became so indistinct that Jolly was reminded of general paralysis. All voluntary muscles were readily exhausted and Jolly noticed that exhaustion of one group of muscles was seen to produce asthenia in others. The child was always better after rest, particularly in the morning. While eating he had to stop frequently because of weakness in chewing; speech became indistinct if he read aloud, but he did not become "mute as a fish"; dysphagia was not present.

Jolly thus was the first to analyse the reaction of muscles in myasthenia gravis to electrical stimulation and to name the disease. He also suggested physostigmine as a form of treatment, but he does not seem to have followed out this important point and it was left to Walker 40 years later to demonstrate the therapeutic value of this drug.

Pineles (1895) added reports of four more cases, one with rapid onset in a man of 25. Two of his patients died

9. Goldflam, S.: Ueber einen scheinbar heilbaren bulbärparalytischen Symptomencomplex mit Betheiligung der Extremitäten, Deutsche Ztschr. Nervenh. **4**: 312-352, 1893.

10. Jolly, F.: Ueber Myasthenia Gravis Pseudoparalytica, Berl. klin. Wchnschr. **32**: 1-7, 1895.

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suddenly of dyspnea, justifying, as had many others, the correctness of the term "gravis" in the designation of the disease given it by Jolly. Pineles seems to have been the first to refer to myasthenia gravis as the "Erb-Goldflam bulbar symptom complex."

Up to 1895, all the reports of cases had come from England, Germany or Austria, the majority stimulated by the pioneer work of Erb, Goldflam, and Jolly. Soon case reports began to come in from France, from Italy, and from America. The first from France came from Charcot's old clinic in Paris, where Marinesco found some recent hemorrhage beside the aqueduct of Sylvius and in the vagal nuclei post mortem in a case formerly observed by Charcot and Brissaud. The brief report was issued two years after Charcot's death under the name of both authors, Charcot and Marinesco (1895). No mention was made of any previous descriptions; the disease was not named.

Murri (1896) [11] reported the first case of Italy under the name of Erb's disease. He used the electrical reactions described a year before by Jolly, and pointed out, in addition to Jolly's observations, that, even when complete exhaustion was produced by an electrical current, the muscles could readily contract voluntarily. He also showed the reverse, namely, that muscles exhausted voluntarily would still react to the electrical current. His paper was illustrated by a series of myograms, exquisitely reproduced and far superior to those found in Jolly's paper in 1895. He was much influenced by Mosso, the Italian physiologist, who had long been interested in myograms. Murri also noted the daily variation in his patient's symptoms.

Another case was added to the literature by Strümpell (1896), who observed a girl, 21 years of age, from Dec. 30, 1893, until her death on March 27, 1894. Particular attention was called to the rapid exhaustion of the muscles and to the fact that the patient was worse during her menstrual period, the first indication in the literature that the disease might be affected by glandular activity. For the last three months of her life, the patient had almost daily attacks of dyspnea, with marked salivation. Death occurred from respiratory paralysis. Postmortem examination, particularly of the medullary nuclei, revealed no abnormalities.

Silbermark (1896) described a cook seen in Nothnagel's Klinik. The patient had noticed, while rolling dough, that the third and fourth fingers were weak and could not be normally extended. Later bulbar symptoms developed, with variations in intensity and duration. He always felt better in dry, warm weather. There were notable remissions.

The symptoms in the patient seen by Devic and Roux (1896) were chiefly neck weakness and ptosis, without other bulbar involvement. They report an excellent remission, followed by a mild relapse. At the same time, Fajersztajn (1896) was observing a man of 23 in Lemberg, who was so sick that he could not sit up in bed and even lifting a spoon to his mouth soon tired him. After six months in bed, improvement followed, but there were transient relapses.

The first paper from America, although not the first report of an American—for Hoppe had already written his paper at Oppenheim's Berlin clinic—is that of Collins (1897),[12] given as a clinical lecture in 1896. Collins reviewed the literature and presented a patient, aged 27, whose first symptom developed during pregnancy.

Kalischer (1897) also reported a case in a man of 50 in whom ptosis developed after an attack of influenza. Dysphagia, dysarthria, and general weakness were later noted, with a positive Jolly test. Kalischer thought there was an affection of the motor nuclei and used the term poliencephalomyelitis. He stressed the possibility of sudden respiratory paralysis after a remission.

Two cases were excellently described by Kojewnikoff (1897) of Moscow. The first, a man of 54, had marked weakness in chewing and swallowing, and tube feeding was resorted to. The patient died suddenly of respiratory paralysis. His second case is of more importance because of the use of the ergograph to test muscular weakness. A girl of 17 first noticed symptoms of a bulbar type at the onset of menstruation. The disease progressed by remission and relapse. During a relapse on one occasion she became dyspneic during sleep in an attack that lasted three hours, followed by recovery. The patient was tested for muscular weakness by the Jolly method and also by the use of the Mosso ergograph. Pulling a weight of 400 gm. with the third finger, once a second, caused rapid myasthenia.

Karplus (1897) separated from the general group of asthenic paralyses those with ophthalmoplegia as the first and most persistent symptom and called them asthenic ophthalmoplegia. In his patient, aged 24, other symptoms did not develop until after nearly 20 episodes of intermittent ptosis and diplopia, when she had general weakness and difficulty in chewing.

The first case in which a postmortem examination was done in America was that reported by Berkley (1897) [13] from Johns Hopkins Hospital. The patient had symptoms for seven years, dying suddenly. No changes were found in any of the motor cells. The case, while atypical, had many of the classical features of myasthenia gravis.

Widal and Marinesco (1897) observed a patient, aged 31, with acute bulbar paralysis. The onset was rapid, and, although there were some variations in the symptoms in the two weeks that the patient lived, the ptosis, diplopia, dysarthria, dysphagia, and general weakness never cleared up entirely. The symptoms were all worse in the afternoon and evening. Chromatolysis of the motor cranial nuclei and of some of the anterior horn cells was found on postmortem examination. The rapid onset, with death in two weeks, plus the changes found at autopsy, make the diagnosis uncertain. Similar cell changes are seen oftener in cases of acute ascending paralysis (Landry's syndrome).

Cohn's patient (1897),[14] a girl of 16, who died after a few months of illness, had a rapid, nonremitting type of myasthenia gravis. At autopsy hemorrhages into the brain stem of a petechial type were demonstrated. It was Toby Cohn who fixed the name of myasthenia gravis given to the syndrome by Jolly.

11. Murri, A.: Sur un cas de maladie d'Erb, Arch. ital. biol. **25**: 64-92, 1896.
12. Collins, J.: Asthenic Bulbar Paralysis, Int. Med. Mag. **5**: 203-212, 1897.
13. Berkley, H. J.: Asthenic Bulbar Paralysis (Strümpell), Johns Hopkins Hosp. Rep. **6**: 94-108, 1897.
14. Cohn, T.: Ueber Myasthenia pseudoparalytica, Deutsche med. Wchnschr. **23**: 785-789, 1897.

Schlesinger (1897) reviewed all types of bulbar paralysis seen at the University clinic in Vienna and found only one case of a doubtful nature. Brissaud and Lantzenberg (1897) gave a full review of the literature on myasthenia gravis and reported one questionable case. Eulenburg (1898) observed a patient for three years with intermittent ophthalmoplegia, and Wheaton (1898) reported a fatal case, without autopsy, from America.

Of more importance was the case reported by Mailhouse (1898),[15] for his patient was a boy, aged 2 years and 9 months, the youngest patient observed and reported on up to that time. The child, who had been healthy previously, died suddenly after a month's illness. There was no autopsy, but the clinical description of myasthenia was unmistakable. In Karplus's case symptoms had supposedly begun at the age of 5, but Mailhouse actually observed the disease before the age of 3. The brief duration before death was also a feature of Wheaton's case.

The subject was again reviewed, this time in Frankfurt, by Laquer (1898), with abstracts of previous cases and with the addition of a case of his own. He noted that the symptoms in his patient became intensified after an attack of bronchitis; the man, aged 49, tended to fall asleep after the midday meal and, as the disease progressed, considerable atrophy developed in the arm and leg muscles. Some muscles were also tender to pressure. The myasthenic reaction was present. As the patient had long suffered from gout, the atrophy and tenderness may have been due to neuritis or myositis and not the result of the myasthenia.

Saenger (1898) noted an improvement in his patient when she became pregnant, but details are lacking in his brief report. Montesano (1898) suggested an infectious element as the causative factor, and Kostezkaso (1898) noted weekly variations in the progress of the disease.

Campbell (1899) demonstrated a case before the Clinical Society of London, Feb. 24, 1899, and Seiffer (1899) another before the Berlin Society of Psychiatry and Neurology on Nov. 13 in the same year. At the latter meeting, the syndrome was discussed by Oppenheim, Bernhardt, Jolly, Kalischer, Remak, Mendel, and Toby Cohn. The name myasthenia pseudoparalytica (Jolly) was generally accepted, as had been suggested by Cohn two years before.

In America, two cases were reported at the 25th annual meeting of the American Neurological Association in 1899. Sinkler (1899)[16] was the first to show the facial appearance of a patient, a woman of 37, by photographs. Ptosis had existed for seven years, but dysphagia and general weakness occurred only after the birth of her sixth child, five months before she was seen by Sinkler. He did not give a clear picture of the patient's condition during the last pregnancy, but the chief symptoms appeared soon after it. Punton (1899), reporting at the same meeting, had observed a woman of 25 with typical symptoms. He was impressed by the "putty-like blankness" of her facial expression.

In discussion, Collins pointed out that his patient, reported on in 1897, was always worse at the menstrual period. His patient also had an acute psychosis of the confusional type.

The year 1900 witnessed a great outpouring of literature on the subject. Cases were reported from many places in Europe and from America. The disease had become widely recognized. In Germany, Feinberg (1900) observed a man of 44, with an unusual onset of intestinal obstruction, occipital pain, and parasthesias. The later symptoms were more typical, and recovery took place in about six weeks. The patient remained well for the next year. Feinberg stressed the onset with "autointoxication." Giese and Schultze (1900) contributed a careful study to Erb's *Festschrift* of a married woman of 24 who had a tendency toward remission and relapse of single symptoms, but never of all symptoms at the same time. She was worse with the onset of menstruation. After a partial recovery, she suffered a psychic shock in the death of her child and immediately had severe dyspnea and other bulbar signs, with rapid relapse and death in two days. On examination, the brain was found to be normal. The authors felt that the disease should be named after Erb. Oppenheim (1900) described a case that was formerly considered as an example of hyperthyroidism or hysteria but later was recognized as a case of myasthenia gravis. The postmortem examination failed to show any changes in the brain cells. After reviewing 19 cases in the literature, all without cerebral lesions, Oppenheim felt that the disease was probably without anatomical basis but that congenital malformation of the brain might play a part in the etiology of myasthenia gravis. In his case he found some minor congenital abnormalities. Cohn (1900) added another case.

In Belgium, two cases were described by DeBuck (1900) and by DeBuck and Broeckaert (1900). In the first case, DeBuck found some atrophy, similar to that found by Laquer, and this caused him to be disturbed about the diagnosis. The other symptoms were characteristic and a diagnosis of myasthenia was finally accepted. The second case, reported by DeBuck and Broeckaert, was more typical of those described by Erb. The Jolly myasthenic reaction was absent, but the authors felt that this was not a constant sign, as had Oppenheim. They found 90 cases in the literature and considered their case the 91st.

In addition to the fine summary by DeBuck, an even more complete review was given by Guastoni and Lombi (1900) of Rome. They observed a patient over a period of nearly three years. He had a scaly, painful dermatitis in addition to many bulbar symptoms. The Jolly reaction was positive. After a number of months, recovery was complete. The authors gave a full discussion of Erb's disease, with a listing of cases previously reported.

In England, single cases were reported by Hall (1900), Guthrie (1900), and Batten and Fletcher (1900). Hall's patient was a woman who was much worse during her menstrual period and in the course of her illness had extreme mental depression. After a partial remission, she died suddenly after eating. The brain sections

15. Mailhouse, M.: A Case of Myasthenia Pseudoparalytica Gravis (Jolly) or Asthenic Bulbar Paralysis (Strümpell), Boston M. & S. J. **138**: 439-441, 1898.

16. Sinkler, W.: Asthenic Bulbar Paralysis, J. Nerv. & Ment. Dis. **26**: 536-544, 1899.

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appeared normal. Guthrie's patient, a woman, aged 23, showed considerable variability in her symptomatology; she could eat breakfast well, but other meals were taken with difficulty. As in the original case of Willis, after she read a few lines aloud, her speech became unintelligible. The case was similar to Campbell's that was presented before the same society in 1899. Batten and Fletcher also observed the disease in a woman, aged 22, who lived only a few months. Death came after eating, in spite of artificial respiration and tracheotomy; the brain sections showed only slight abnormal signs in the cranial nerve nuclei.

Buzzard (1900) reported on one case in a man, aged 40, who had symptoms for seven years. With rest, his symptoms almost entirely disappeared. His second case, in a woman, aged 24, was also not severe. The Jolly myasthenic reaction was present in each patient.

Campbell and Bramwell (1900) [17] reviewed the entire literature up to 1900, abstracted each case, and compiled a table giving the major symptoms and signs. Although they made a good many minor errors in tabulation, the paper was important, for it served to fix the main concept of the disease in the minds of the men in the British and American medical profession.

During 1900, two more cases were reported from America, one by Brown (1900) and another by Paul (1900).[18] Brown's patient, a woman, aged 29, was ill about 16 months; she lost 15 lb. (7.3 kg.) in weight and was greatly reduced in strength. She experienced a good spontaneous remission. Inability to do her hair was one of her chief symptoms. In the discussion of Brown's paper, four more cases were noted briefly by the physicians. Paul's patient, a 23-year-old woman who had been married for three years, had many typical features of the disease. This was the first case reported from the Massachusetts General Hospital. Following is an account of the symptoms based on the original clinical history:

Eight months before presenting herself at the hospital and 18 months after her confinement, while taking the part of a Japanese girl in private theatricals, she stooped low, in a line with a number of other performers; at a given cue all the line were to resume the standing attitude, but the patient could not rise and asked for help. She was ridiculed a bit and then assisted to stand. In the final performance she received assistance from her comrades on either side and suffered no further disability. Ascending stairs became difficult; in boarding a car she could not lift her feet without assistance. If merely helped in the usual way by taking of her hand or arm, she would be pulled forward and fall on her face. This loss of muscular power was of brief duration. Crossing the knees at times required assistance. She could usually walk on a level, but stepping up was frequently difficult. In spite of her myasthenic symptoms, she attended to her housekeeping and cared for her baby.

Transient weakness in the arms next appeared; at times they would drop like lead without sensory disturbance; her husband had to support them when she arranged her hair; to insert a hat pin she rested the elbows on the mantel. In playing the piano both hands tired easily. She would sometimes have to drag the baby to her lap rather than lift him clear. Once when she was attempting to take him from his crib it was impossible to straighten up until assisted. She refrained from handling objects. There was difficulty at times in buttoning, and ability to do millinery and embroidery was lessened. The attacks of weakness became more frequent. These symptoms were of short duration and came on usually after severe use of those muscles in which weakness or complete loss of power developed. She not infrequently fell backwards on stairs, and on one occasion when near the top her legs gave way and she fell with the baby in her arms, sliding down several steps without injury. Transient diplopia occurred in the course of the disease, and it was noticed at times that when she looked up the head was thrown back, indicating ptosis. The muscles of mastication escaped. There was lack of expression in the face, and the laugh seemed incomplete. The voice at times was nasal and somewhat indistinct, though not lowered. Words were correctly chosen, and speech was never really lost. One day the words ran together and the lips seemed powerless, but holding of the upper lip with the fingers obviated her difficulty. Swallowing was sometimes awkward, and in the later stages this difficulty became serious. The neck muscles sometimes suddenly gave way so that the head required support.

The symptoms became more frequent, and involved on several occasions very nearly all of the voluntary muscular system. One evening six months before death, after climbing the stairs safely, she fell to the floor unable to move or speak, but finally succeeded in attracting attention by tapping the floor with her heel. Later, in attempting one day to step up on the piazza, she fell in a heap and had to be carried bodily into the house. In a third instance, five weeks before death, she fell helpless at the top of the stairs. After a few moments she regained control of her muscles in each instance; some drowsiness followed the last attack, but no unconsciousness.

The most serious symptom to develop was choking, the first attack occurring about six months before death. At the commencement of a meal, the first attempt to swallow water caused strangulation; she became cyanosed and unconscious, but revived at the end of about 30 minutes. A month later, after she took two swallows of water without trouble, the third choked her. Cyanosis and unconsciousness followed, and Dr. Campbell, who was present, seriously considered tracheotomy. Such attacks and the accompanying apprehension impaired nutrition materially, but there was no local atrophy. Her mind remained clear. Palpitation and dyspnea occurred, but were not prominent symptoms.

There was no numbness or prickling. Appetite and digestion were good. The disposition was unaltered; the catamenia reappeared after confinement and did not modify the symptoms. The sphincters were unaffected; there was no spasmodic movement, stiffness, or tenderness. Emotional excitement aggravated the disturbance.

During the last few months of life the attacks of weakness became more frequent and profound, yet, when seen in the intervals, she gave no impression of serious illness. The bulbar symptoms became more pronounced and at

17. Campbell, H., and Bramwell, E.: Myasthenia Gravis, Brain **23**: 277-336, 1900.

18. Paul, W. E.: Case of Myasthenia Gravis Pseudoparalytica, Boston M. & S. J. **143**: 632-634, 1900.

one time rectal feeding was practiced; but the ability to swallow food and liquids returned while she was at the Boston City Hospital, some months before death. Toward the end she was sometimes unable to roll over or to sit up in bed, showing involvement of trunk muscles.

The ocular symptoms also increased, but there were remissions with apparent normal muscular balance. Exposure to cold did not aggravate the condition, as a rule; but once, on leaving the car after a journey, she became helpless on encountering the chill of a March air. Three days before death she was able to try on a dress, and two days before death she sat in a chair and swallowed without trouble. At this time she complained of palpitation and of a sharp pain in the right iliac region. The lungs filled up but became clear again after several hours; there was temporary inability to spit out or swallow the secretions. Death occurred 18 months after the first symptoms.

SUMMARY AND CONCLUSIONS

From 1672 to 1900 the concept of a disease, myasthenia gravis, was formed in the minds of a score or more of medical observers. Willis, the first of a distinguished line, grasped the essential clinical signs and delineated their identity in 1672. His description died aborning until uncovered by Guthrie in 1903, although it may have lingered smoldering in the minds of physicians in the 18th and 19th centuries, even to the point of influencing practice by a vague recognition of a specific disease. Nearly 200 years after Willis wrote his discerning note, another English physician, Wilks, in 1877 gave a brief account of a girl with symptoms suggestive of myasthenia. Although the history of his patient's illness is not entirely characteristic, difficulty in swallowing, talking, and breathing developed rapidly, and death occurred suddenly. At postmortem examination no microscopic changes were found in the medulla, strikingly in contrast to what was already common knowledge of the pathology of bulbar paralysis of the degenerative type. Wilks thus contributed the initial description of the failure to find pathological destruction of nerve tissue in the appropriate area of the central nervous system. Wilks' account, as had that of Willis', passed almost unnoticed. Two years later however, Erb in Germany wrote a reasonably full account of the syndrome based on the observation of three patients, one of whom died suddenly. An even more complete single case history was contributed by Eisenlohr in 1887, and subsequently within a few years many other reports were at hand, including an unusually detailed one by Hermann Hoppe, an American student working in Oppenheim's clinic in Berlin in 1892. Goldflam (1893) added greatly to the growing concept of the disease, and his name is rightfully linked with that of Erb in the eponym, the Erb-Goldflam symptom complex. Jolly (1895) was the first to use the name myasthenia gravis and he added the term pseudoparalytica because of the lack of structural changes found post mortem. This name was generally accepted at a meeting of the Berlin Society of Psychiatry and Neurology, held Nov. 13, 1899, a meeting attended by Oppenheim, Jolly, and many others. Two cases were reported at the 25th annual meeting of the American Neurological Association in 1899 by Sinkler, who was the first to demonstrate the facial appearance of a patient by photographs. The year 1900 witnessed a great outpouring of literature on the subject. The disease became widely recognized in the minds of the British and American medical profession, chiefly owing to the paper by Campbell and Bramwell in *Brain*, a standard neurological journal. A typical case, seen at the Massachusetts General Hospital, was described by Paul in 1900.

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COUNCIL ON FOODS AND NUTRITION

COUNCIL ON FOODS AND NUTRITION

This article was written at the request of the Council by the worker who first described kwashiorker as an entity—Dr. Cicely D. Williams. Its publication in THE JOURNAL *will direct attention to this syndrome, which is known to exist in wide areas of the world—Africa, Latin America, Mexico, Central America, the Caribbean Islands, and elsewhere—and which may occur, but be unrecognized, within the boundaries of the United States and its possessions.*

JAMES R. WILSON, M.D., *Secretary.*

KWASHIORKOR

Cicely D. Williams, D.M. (Ox.), F.R.C.P., D.T.M.&H. (Lond.), Mona, Jamaica, B. W. I.

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The study of child health is of comparatively recent growth in the scientifically advanced countries. It is still rudimentary in the countries that are relatively underdeveloped. In most tropical areas, the first duty of the "imported" doctors was to care for the imported population and then to control the major epidemic diseases that might endanger the people as a whole. Preventive medicine was mainly concerned with mass methods. Gradually, more of the indigenous people began to appreciate western medicine and began to accept and then demand treatment.

Tropical diseases are, in fact, mainly due to poor standards or personal hygiene and poor environmental conditions—not to climate. But tropical medicine is overburdened with entomology and laboratory pathology. Even now, courses offered in tropical medicine contain little reference to children. Books on tropical medicine are equally negligent, although it is well known that infancy and childhood are the ages at which adverse environment is most devastating.

When child centers were first started in tropical countries, they were looked upon as amateurish and fanciful. Many persons regarded them as unnecessary frills and not as the basic need of a medical service. Few persons realized that "the survival of the fittest" is a misapplied cliché. It was not recognized that the same conditions that will kill 30% of the babies in the first year of life will also produce a large proportion of persons with damaged lives who will be a burden for years and perish at a later date.

THE DISEASE IN AFRICA

Child welfare clinics were started by the colonial medical service in the Gold Coast, West Africa, during the second decade of this century. The original idea was that they should prevent disease but not cure it. It did not at once occur to anybody that this type of child welfare center was designed to meet only felt needs in a population that already possessed an efficient and acceptable curative service during an era when the value of follow-up was not appreciated. These centers soon became extremely popular, but it was obvious that the demand for treatment of sick children was over-

Because of lack of space, the bibliographic references have been omitted from THE JOURNAL and will appear in the author's reprints.

whelming. As soon as the Africans discovered that here were physicians who were particularly interested in children, they brought them in swarms. Children's hospitals were built in the two main towns, Accra and Kumasi. The legend was that these hospitals would only take in patients with minor nutritional disease, while patients with serious disease would be sent to the general hospitals. The parents would accept treatment, including admission to a hospital, at the children's centers, where they had learned to know and trust the staff, but many simply would not consider going anywhere else. Fortunately, the mother always insisted on staying in the hospital with the child. "Rooming in" and "demand feeding" were practiced in the Gold Coast long before they were discovered in other countries.

The doctors in charge of these children's centers were faced with many problems. They were officially urged to do prevention rather than treatment. But they realized that disease cannot be prevented unless one knows something about what one is trying to prevent. Their European experience and books were useless, and opportunities for laboratory investigation were minimal. But there was much to be learned simply by observing the children and by talking with the parents and with the African staff. Once they found that the physicians were interested in children, their cooperation was boundless.

It was soon evident that malnutrition was a big problem, though poverty was not. There was little real shortage of money or of food, but there was deep ignorance of how a child should be fed, of how to exploit available resources, and of how to preserve supplies from the season of plenty to the season of shortage.

Few patients presented a simple problem. The doctors had been brought up to avoid a "double diagnosis." Malaria, however, was almost universal, and the incidence and mortality were highest at the ages of 6 months to 4 years. Roundworms were common, and up to 90% of some groups were infested. Yaws, scabies, tropical ulcers, septic skin infections, diarrhea, dysenteries, and respiratory infections were all abundant. Sometimes a patient would be suffering from six or eight of these conditions all at the same time. It was under these circumstances that cases of a spectacular and often fatal form of disorder began to sort themselves out.

In 1927, Dr. R. A. W. Proctor [1] had written in the *Kenya Medical Journal* of a hitherto undescribed condition: "The disease occurs only in quite young children; the child is almost always of an extraordinarily light color and is usually brought up on account of swelling of the feet. The only history obtainable appears to be that in a number of cases there had been slimy motions for some time. As the disease progresses the child becomes paler in color and the pigment appears to be concentrated into a curious black desquamation which is most noticeable on the arms and legs; cracks and sores are often seen at the bends of the elbows and knees, and there may be general edema. The child, as far as my information goes, nearly always dies."

In 1906, Czerny and Keller [2] described a condition among children in Germany due to excessive carbohydrate in the diet, which they called *Mehlnahrschaden*. The disease was obviously close kin to the one we were seeing in the Gold Coast. This was recognized by Waterlow [3] after extensive research some years later. In 1932, a similar condition in West Africa was described by Dr. M. Licurade [4] under the title "Les enfants rouges du Cameroun." Unfortunately, none of these publications had made their way to the Gold Coast, and we were unaware that the condition existed in other parts of the world.

The disease was first noted in the south, or "colony," part of the Gold Coast. Since the supplementary food for children in that area was nearly always some form of white maize and since some of the features of the disease were comparable to pellagra, it was thought that the maize might have a causative relation. The first article on the subject was published under the title "A Nutritional Disease of Childhood Associated with a Maize Diet." [5] Later, it was found that the condition was also prevalent in Ashanti, where maize was not the only supplementary food; therefore, in a short summary for *Lancet*,[6] it was called kwashiorkor. This cumbersome word was merely a confession of ignorance. It was the name given to the disease by the Accra people, to whom it was well known. Some say the word means "red Kwashi." Kwashi is the name for a boy born on a Sunday, but it is used as a generic name as we would use Johnny or Tommy. Even now, in Jamaica a simple country fellow is referred to as "Quashie." In this name, I believe the redness refers to the raw areas where the skin has peeled off in the severe and acute cases and not to the hair. MacPherson,[7] on the other hand, believes that, since red is the color of magic and these children are regarded as possessed, the "redness" refers to the *mystique* of the disease. One of the conditions governing the selection of a paramount chief was that he should not have red hair. The supreme virtue of the word kwashiorkor is that it does not make any unwarranted assumptions with respect to etiology or pathology. It was remarked in a *Lancet* editorial that it has the merit of neutrality.

In 1934, Dr. H. S. Stannus [8] wrote an article to the effect that the disease was, in fact, infantile pellagra. Some physicians, with first-hand knowledge of the disease, accepted his assumptions. Further study has generally led to the opposite conclusion; frank cases of the two conditions cannot possibly be confused. But it is obvious that in all types of nutritional disease, mixed cases can occur, and it may be impossible to decide which of the conditions is the dominant type. Soon after this, Dr. H. C. Trowell, working in Kenya and Uganda, began to investigate the condition.[9] At first he accepted the diagnosis of infantile pellagra, and later adopted the name malignant malnutrition. He has now reverted to kwashiorkor. Trowell has made invaluable contributions in the study of the disease and in bringing it to the notice of physicians in many parts of the world. Achar [10] prefers the name nutritional dystrophy.

In recent years kwashiorkor has been described as occurring in every part of Africa, India, China, the Philippines, Fiji, Indonesia, Malaya, South and Central America, the Caribbean Islands, and in Hungary and Italy. In such diverse backgrounds and food patterns, it is obvious that there are multiple factors that may complicate and variegate the picture. The areas where rice or wheat form the main bulk of the diet do not appear to be as subject to the disease as those where maize and root vegetables, such as cassava, yams, sweet potatoes, and Colocasiae are the staple foods.

In 1949, the joint committee on nutrition of the Food and Agricultural Organization (FAO) and World Health Organization (WHO) reported as follows: "One of the most widespread nutritional disorders in tropical and sub-tropical areas is a syndrome, at present ill-defined, known by various names such as 'kwashiorkor,' malignant malnutrition, poly-deficiency disease, 'm'buaki,' 'syndrome dépigmentation oedeme,' infantile pellagra, etc. The committee is satisfied that this condition is not identical with classical pellagra and suggests that the name 'infantile pellagra' should not be used for this syndrome. It appears that the highest incidence of the disease occurs in infants and young children and that the mortality rates in some parts of Africa are disturbingly high." The committee "recommends that WHO conducts an inquiry into the various features of kwashiorkor . . . to define the clinical features and to study the food habits of the population." As a result of this, Drs. J. F. Brock and M. Autret made an investigation and published a report on the condition as it was seen in Africa.[11]

The disease is obviously not a simple one, and it is impossible to produce a simple definition to please all tastes. It is probably due to malnutrition and most likely to some protein defect or defects. There are bound to be many local variants. The presence of intestinal parasites, of mineral, vitamin, or other defects, and concurrent infections will produce modifications. When the disease was first described, the severe, spectacular cases were the main theme, physicians are now able to detect the early cases—the slight swelling of the dorsa of the feet, the slight enlargement of the liver, the mild anorexia, the apathy, and the coldness of the extremities—which in the early days would have been missed or underrated. In fact, a name means very little except to classify a certain conception. Until the pathologists and biochemists can give us more precise information about the defects, we may as well accept the word kwashiorkor in all its cacophony.

In recent years the literature on kwashiorkor and kindred conditions has reached vast proportions. Now that it is receiving worldwide attention and there is more opportunity for exchange of information, it is possible, to some extent, to keep track of the observations in a number of countries. But much confusion is due to misquotation, failure to study references, and the inaccessibility of relevant literature. An excellent summary by the late Professor Altman, published in 1948, is useful.[12] He gives 84 references to literature from 12 countries up to that date. Brock and Autret[11] give a wide but incomplete bibliography. In recent years, most of the papers are reviewed in journals of nutrition and of tropical medicine. They are mainly neglected by the pediatricians, who have not yet attained any degree of geographic versatility.

HISTORY

Invariably the history is of a low protein diet. In the Gold Coast the disease is described as "the sickness of the deposed baby"; that is, it is associated with weaning. In some cases, the breast feeding was inefficient. The mother was sick or was dead, and breast feeding was undertaken by an aunt or a grandmother who had not had a baby for some years. In one case, it was a grandmother whose youngest child was 19 years old. In East Africa, where the condition is much commoner and where the average diet of the population is much worse, the babies start to show the symptoms when they are still being breast fed. This also applies to India. Thus far, the composition of the mothers' milk has not revealed consistent abnormalities, but this subject requires more attention. Certainly, in many of the early cases, the mother's diet has been noticeably poor in proteins. In many parts of Africa, there is little or no cow's milk to be had; in India, even if the cow's milk is available, the animal may be in exceedingly poor condition, and the milk is again from a malnourished source.

The fact that many other children in the community have a low protein diet and have mothers who have a low protein diet and yet do not suffer conspicuously from kwashiorkor is typical of most nutritional stories. There is obviously enormous individual variation in capacity to absorb and utilize the available diet. It often happens that the disease does not become evident unless some added factor such as roundworm, hookworm, or bronchitis is acquired and tips the balance. It is suspected that some persons recover without obvious external signs but with liver damage that may be crippling or fatal in later years.

RETARDED GROWTH AND MENTAL APATHY

Growth is always retarded, even though the child, at first, appears neither emaciated nor ill nourished. In the areas where the disease is rampant, it is found that the weight curves of Kampala (East African),[13] Gambia,[14] and West Indian [3] babies follow the same curves as those of European infants up to about four months and then begin to fall. This symptom, of course, is not specific. If children are regularly observed, as they are at welfare centers, growth failure will be found to precede some attacks of beriberi [15] and many other diseases.

Peevishness and apathy may be the first sign to develop. The child becomes stolid and indifferent. He shows none of the interest and liveliness that are normal to a well-nourished child. If disturbed, he becomes resentful and peevish, but he shows no vigor in his resentment. As the disease progresses, he sinks more deeply into a state of depression and resentment. One of the earliest signs of improvement is that he begins again to show complaisance and then interest or pleasure.[16]

EDEMA

Edema may be a very early sign. Sometimes, in the Gold Coast, the mother would begin to notice a very slight swelling on the dorsa of the feet and then of the hands. When the edema is more generalized, it may mask a severe degree of emaciation. Generally the edema is more marked on the extremities than on the trunk. When there is edema of the face, it is generalized. There is no marked puffiness of the eyelids, as in nephrosis, and there is no marked pendulousness of the cheeks, as in ascariasis. Edema does not usually become extreme as it may do in cases of nephrosis and beriberi. In fact, an injection of thiamine can be used as a diagnostic measure in cases of doubt or when a mixed condition is suspected. Beriberi will respond promptly with a diuretic deluge. The edema of kwashiorkor generally disappears slowly as the child recovers, but in most fatal cases it also decreases before death. Edema may be present at the same time as emaciation. The moribund patient is not always edematous and not necessarily emaciated.

HYPOALBUMINEMIA

In the early descriptions of this disease, there was no opportunity to record blood chemistry; however, various observers have made extensive studies. In the majority of cases it is found that the serum albumin is low (down to 2 gm. per 100 cc.), while the globulin is extremely variable. It has been found that many persons, even children, may have the same, or almost the same, anomalies of serum proteins, without having obvious kwashiorkor.[17]

Dean [18] has summarized the blood findings: "In the serum of these children the total proteins and the albumin were considerably below normal in amount but the globulin was high. . . . The blood urea was little more than half the normal figure and the total cholesterol was also very low. The ratio of free to total cholesterol, which depends on an enzyme, a cholesterase, whose activity was presumably greatly reduced, was very high, and other enzymes seemed to be affected in the same way; alkaline phosphatase, cholinesterase, amylase, and total esterase were all low. . . . The height [of globulin] at the start and at the end of treatment are both due to γ globulin, the α and β globulins are less affected. The albumin rises more than the total globulin so that the albumin/globulin ratio rises, but it seldom goes over unity."

Anemia is not an essential part of the disease. In many cases it is insignificant. But children very often react to malaria with rapidly developing anemia,[19] and the anemia that accompanies roundworms in young children can be as severe as that seen in cases of hookworm infection.[20]

DYSPIGMENTATION AND DERMATOSES

"Dyspigmentation" is preferred to "depigmentation," since the hair not only is bleached but is also changed to a reddish color. The hair changes are not specific. It is well known that any form of wasting disease may affect the color and texture of the hair. Exposure to sun, wind and rain, and salt water may also produce changes that are very similar. In West Africa there are persons of pure African ancestry who have red hair and are in good health.

In East Africa the hair changes are common and range from slight softness, or reddish tone, to hair that is dry, straight, sparse, staring, and red, pale, or bleached. In Indian children the hair may be reddish, gray, or white. In many cases of mild nutritional defects, a slight reddish fringe may be seen over the forehead and around the temples. In some of the very acute cases of kwashiorkor seen in the Gold Coast, the hair changes were not conspicuous. Some of these cases were rapidly fatal. It may be that the hair changes may partly depend on a variable mineral depletion. They certainly vary enormously with racial background. It is important to regard the hair changes in the right perspective. If a pigmented 2-year-old baby who has not been exposed to the elements and who is not suffering from tuberculosis or another wasting disease has hair that is dry, pale, sparse, and staring, he is probably suffering from some degree of malnutrition of the kwashiorkor type.

The skin changes are the subject of much controversy and should be considered together with other nutritional dermatoses. In the Caucasian race it has long been recognized that unhealthy persons will not pigment normally on exposure to sunlight. In the pigmented races also, the color and texture of the skin are an important signpost. In many children of pigmented races, wasting diseases are accompanied by pallor. In cases of kwashiorkor this is often well marked. Trowell has noted that very often the pallor on the face is more marked than on the rest of the body. In many persons of pure Negro ancestry reddish hair and skin will develop.

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The cases referred to as kwashiorkor by the Accra people were in children who had dark thickened patches of skin on limbs and back, which peeled off, leaving a pink, almost raw surface. Later it was noted that in some countries children seemed to be suffering from the same type of disease, but the skin did not proceed to this dramatic development. In some cases the perineum was the only, or the main area affected. "Crazy pavement" [5] has often been used to describe this condition, but it is not particularly apt. I would suggest instead "peeling pellagroid" to indicate the depth of the desquamation. In fact it is extremely difficult to handle these children without major trauma. Besides soft thickened patches that on peeling leave a raw surface, there is often a generalized desquamation, extending over the trunk.

Severe cases are often accompanied by angular stomatitis and desquamation at the outer canthi, which may be due to some degree of concomitant ariboflavinosis. There may also be photophobia and corneal ulceration. There is often glossitis and buccal ulceration. In the countries where kwashiorkor is commonest, there are also many cases of cancrum oris, and the two are sometimes found in the same person.

In areas where there is much malnutrition, often a glossy dryness is found on the extensor aspect of the tibia. This proceeds to a superficial cracking of the skin and, in the later stages, to a pigmented mosaic appearance that is found mainly in growing children and in adults. The same may appear on the forearms. But this condition is found in places where kwashiorkor is rarely seen; of course, mixed conditions may occur.[21]

It may be that variations in the fat or some mineral content of the diet are concerned in the development of the skin changes.[22] In some instances the skin changes are inconspicuous; in others they are startling. One of the most distinctive points in diagnosis lies in the photosensitivity of the skin in pellagra. In kwashiorkor the lesions may appear on, and be confined to, the areas protected from the light.

GASTROINTESTINAL DISORDERS

Gastrointestinal disorders again are inconstant and irregular. The earliest sign is anorexia. The patient may refuse food or may show a lack of initiative with respect to food. The anorexia may become an extreme problem in treatment. Vomiting is common. Sometimes a child will stolidly go through a meal, quietly vomit the whole lot, and then curl up in bed exhausted and withdrawn. Attacks of diarrhea may alternate with constipation. The stools may be merely loose and slimy or may be those of steatorrhea. There is rarely any blood. Attacks of diarrhea and/or vomiting may delay recovery. Nutrition must be improved with caution.

Ascariasis is common in many parts of the world where kwashiorkor is found. Some observers hold that one depends on the other. Until the present time not nearly enough attention has been paid to the devastating effects of ascariasis on the young child.[23] The infection can be acquired at any moment after birth from the dirty hands of the mother or other attendant, whereas ancylostomiasis does not generally occur until the child is old enough to toddle in places where larvae lurk. One or two male ascarides in the intestines of a young baby may produce no ova but may cause havoc in the digestive system or even death. In countries where there is a high rate of ascariasis, adults who may harbor many helminths in apparent symbiosis will be found. But the effect on the children, who have not yet acquired an immunity, is very different. If a child gets sick, the roundworms often leave the host. In an acute illness, the worms can be observed leaving by any of the orifices and often cause intestinal obstruction if they are in large numbers. In a chronic disease, the "rats may have left the sinking ship" before the child comes under observation. Ascarides may be a factor in the case, although all the worms have departed, and they are certainly an important factor in a large proportion of the cases of kwashiorkor in certain parts of the world. Ascarides may cause liver abscesses and possibly other liver damage.

PATHOLOGICAL CHANGES

Pathological changes are mainly in the liver, and enlargement, fatty infiltration, necrosis, and fibrosis occur singly or in combination. The typical necrosis is cellular, that is, seen only on microscopic section.[3] The liver is generally enlarged. It will go through a stage of considerable enlargement, but in many advanced cases it is shrunken, soft, and so fatty that it is almost diffluent.

There is great variation in the size of the normal liver. Mitchell and Nelson [24] state: "in the newborn infant the liver edge is about 5 cm. below the costal margin in the right midclavicular line. . . . The lower border of the liver may be palpable normally below the subcostal margin throughout childhood." Judging by the frequency of diabetes and Fröhlich's syndrome, American children must suffer more from overfeeding than from underfeeding. Apparently both forms of malnutrition may produce enlarged livers. Most observers in Europe would not agree that the average child of 18 to 24 months had a liver below the costal margin, while in malnourished countries a palpable liver at this age must be regarded as suspect. It is difficult to determine exactly what amount of fat in the liver of a child may come within normal range. Waterlow [25] gives 4 to 5% as normal, but he has found that children with kwashiorkor may have up to 30% of fat even before there are gross external signs.

In the earlier studies of kwashiorkor [26] a fatty infiltration of the liver was the most constant and the only conspicuous defect. In some of the more chronic cases, the fat seemed to be disappearing, and the liver was flabby, with extensive necrosis. In most of the later work the changes in the liver have been far more carefully studied. Waterlow [27] has found all stages of fatty change in the West Indies; however, the babies in the Gambia began to have fibrosis at extraordinarily early stages, without any previous fatty degeneration. Jelliffe and Silvera [28] have found fatty livers present in the early weeks of life long before other symptoms had developed, so the disease may start as intrauterine malnutrition. With the development of the techniques of liver biopsy, it is now possible to study these diseases far more accurately, and this will lead to better definitions and more specific treatment and prevention. Waterlow [27b] first described the atrophy of the external secretory cells of the pancreas. Davies,[29] in an important study of the pathological changes, described fibrosis of the pancreas as well as of the liver. He believes the pancreatic lesion to be the primary one.

OTHER FINDINGS

Trowell and Thompson [30] have done some extremely careful and interesting work. Taking edema, without obvious renal or cardiac cause, hair changes, and subnormal weight as the criteria for diagnosis, and using normal African children for comparison, they found a well marked reduction in amylase, lipase, and trypsin that was reversed with a high intake of milk protein. Veghelyi,[31] working in Budapest, has also described the defective enzymes.

In the Gold Coast patients coldness of the extremities was very important. Even in an equatorial climate this sign was conspicuous. Keeping the child warm was found to be one of the most important points in treatment of all the advanced cases. A radiant heat cradle would facilitate recovery in no uncertain degree.

LATE RESULTS AND DIFFERENTIAL DIAGNOSIS

Cirrhosis and carcinoma of the liver are common in some of the countries where kwashiorkor is found. What the exact relation is between these conditions has not yet been proved. Infantile hepatic cirrhosis developing into portal cirrhosis, so common in India and Ceylon,[32] and serous hepatosis, probably related to it, described by Hill [34] in Jamaica, are also very likely to be of nutritional origin. The place of infection, such as infectious hepatitis, in this picture is not yet clear. In these cases, the patient looks well nourished and cheerful. Ascites may be an early sign. The liver is enlarged and hard, but biopsy shows no fat. There is a typical exudate that leads to fibrosis. Of course, some mixed cases occur.

Brock and Autret [11] give the following definition of the disease: "A nutritional disorder occurring particularly in the age period six months to five years . . . associated with low protein diet.

The fundamental characteristics of the syndrome are:

1. Retardation of growth.
2. Dyspigmentation of hair and skin.
3. Edema usually associated with hypoalbuminaemia.
4. Pathological changes in the liver including one or more of the following—fatty infiltrations, necrosis, and fibrosis.
5. A heavy mortality if untreated or incorrectly treated.
6. Nutritional dermatosis—occurs in a variety of patterns, but may be absent.
7. Gastrointestinal disorders. These are variable and include one or more of the following—anorexia, digestive upset, diarrhea, mild steatorrhea.
8. Peevishness and mental apathy.

Unfortunately the order is illogical, and this study only refers to Africa; but the statement will serve as a basis for discussion.

Pellagra is the main condition with which confusion is likely to arise. It cannot be stated too often that there is nothing to prevent the finding of mixed conditions. The differential diagnosis was previously stressed,[34] but it may be useful to repeat it.

Kwashiorkor	Pellagra
1. Common in young children	Rare in young children
2. Well-developed dermatitis indicates a severe degree of the disease	Severe dermatitis may occur before constitutional signs develop
3. Rash has no relation to exposed areas	Skin is photosensitive. Rash is only on exposed areas and will disappear if skin is protected
4. In early stages skin may be bleached. No well-marked edge to rash	Early stage of rash is red, swollen, and irritating, with well-marked edge
5. In later stages skin is dark, soft, and crumpled and strips easily, leaving raw surface	In later stages there is a dry, branny desquamation
6. Disease may develop in patients on a diet containing some milk	Disease not described with milk diet
7. Large mortality if untreated	Rarely fatal

Kwashiorkor differs from total undernutrition in that the actual intake of calories may be sufficient, but the excess of carbohydrate in relation to protein is damaging. Other factors are important, such as the various amino acids and the proportion in which they appear in the diet. The disease differs from marasmus in that severe illness and death may take place long before there is emaciation.

Hunger edema generally decreases with rest and often increases after a balanced diet has been started, but has many features in common with kwashiorkor. It is, in fact, a part of the syndrome, but it can exist in adults with a normal liver and with serum proteins only slightly altered. Kwashiorkor is associated with hypoproteinemia.

MORTALITY

In the early days, when the disease was not diagnosed until its late stages, the mortality was high, up to 80%, but since then the condition has been more extensively studied and the mortality reduced. In certain areas the hospitals are still confronted with numbers of patients in the late stages of the disease, many of whom die of it or of some intercurrent condition. In these areas too, it is difficult to maintain follow-up. Even patients who leave the hospital vigorous and, apparently, in perfect health may, a few months later, die of the same disease.

TREATMENT

In early days [35] it was found that patients would respond to milk in the diet, and now it is proved that milk protein is curative if irreversible changes have not already set in. Achar [10] has had good results with blood transfusions and concentrated human serum. Most physicians have found it essential to reduce the edema before much intravenous nutrient can be given. In this the radiant heat cradle is most useful, and when possibility of beriberi is a complication, thiamine injections should be tried. Protein hydrolysates have been used with good but variable results.

Feeding often presents great difficulties. If the child is still breast fed, the mother's diet must receive attention and supplements must be given to the child. If the child is weaned, it may be extremely difficult to induce him to take any other food than the boiled banana (*matoke*) or cornmeal or other food to which he is accustomed. He will often refuse to drink milk. In these cases, milk protein in powder form can be mixed with the accustomed food until the appetite improves. In South Africa [32d] the Gillmans reported good results with dried hog stomach, but this has not been found successful in other places. Nicotinic acid has been reported in some areas to improve the skin condition, but this again is not a universal finding. It must be remembered that the skin condition often improves when the patient does not. Also that in some patients who die, the skin condition may show marked improvement before death, even without nicotinic acid. Assessing results is difficult, because it is not possible to compare relative conditions when the child is admitted to the hospital. In cases of severe anorexia a nasal tube with a slow drip may be used.

It is important to remember that much depends on intelligent and devoted nursing. Warmth, interest, and encouragement are needed, and patience and persistence on overcoming the anorexia. Small, frequent meals should be given, with a high proportion of milk protein and, at the beginning, very little fat. Food yeast or grated cheese added to the milk may make it more acceptable. Dean [33] finds that the patients in Kampala were intolerant of lactose, glucose, sucrose, and maltose but that *matoke*, boiled green bananas, provided a more successful source of carbohydrate. Dean also found that soybean protein could be used instead of milk. This is an exceedingly important discovery for countries where milk is unobtainable or in short supply.

Besides careful attention to general nursing and to diet, the other deficiency diseases must be treated. Anemia, beriberi, and ariboflavinosis are not uncommon. Malaria must be excluded. Platt [36] is of the opinion that these children cannot tolerate antimalaria drugs very well. This also applies to anthelmintics, and deworming must be carried out with the greatest caution. Only by efficient follow-up work through outpatient clinics, dispensaries, and welfare centers in close touch with the hospitals can permanent cures be claimed. It is a waste of time to investigate these diseases or to cure them in hospitals if teaching in the homes and parent education is neglected.

PREVENTION

Kwashiorkor is prevented by a reasonably good diet for mother and child. It is a melancholy reflection on the past defects of tropical medicine that a disease so spectacular and so widespread should have been ignored for so long. World hunger and the rise of communism are the two things most dreaded in the free world. The two are interrelated, and the prevention of kwashiorkor is concerned with the same problems. Investigations on this disease are by no means complete, but we know enough to cure the disease in 95% of cases and to prevent it in everyone. While many of the most able intellects are at work finding out more scientific details of pathology, there are extraordinarily few attempts being made in methods of insuring prevention. Yet if we can prevent kwashiorkor, we can also prevent world hunger and other evils.

Prevention lies in teaching the parents what food to provide for themselves and their children. In many areas this food is not available at present; only comprehensive undertakings that will coordinate agriculture, education, and health can be of any use. In many other areas it is ignorance, prejudice, and wastefulness that is responsible—not poverty.

Disease control projects, relatively easy to apply, have absorbed both the national and the international agencies. The result has been vast increase in populations, without any comparable improvement in the standard of living or education. Blind craving for spectacular results is leading straight to disaster. It is time that medicine realized that its duty is to aim not only for healthy minds in healthy bodies but for healthy persons in a healthy community.

If the medical leaders had any sense of proportion, they would be changing over as rapidly as possible in order to adjust the balance before disaster overtakes man. They would devote their best men and their largest finds to the constructive side of medicine—education toward healthy living, physical and mental, training of personnel, and follow-up—which is social medicine.

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Many persons are doing research in electronics and in the more abstruse sciences. In order to make a balanced world, we should provide far more persons who can and who will experiment in methods of propagating improved mental and physical health. We worry a great deal about the persons we want to liberate from political tyranny, and we ignore those we could and should liberate from the tyrannies of dirt, ignorance, and hunger.

In many parts of the world, maternal and child health work is now established, but too often it is grossly inadequate, both in extent and intent. It is the method par excellence of reaching the parents, the homes, the schools, and of improving the nutrition. This type of work cannot be done on any preconceived pattern. It must be adjusted to the needs and resources of each country. It needs the most careful observation, evaluation, and planning if results are to be achieved. Too often this work is regarded as a mere appendage, to be left to the uncertain care of voluntary societies. It may be scorned by the hospitals, directed by health officers who have no interest in it, and carried out by nurses who have little or no training in pediatrics, nutrition, or social dynamics. "Social welfare" is often engaged in expensive failures because it ignores the needs, the techniques, and the opportunities of health and nutrition.

Child health work is often discouraged by those who are most apprehensive of overpopulation. They ignore the obvious; persons who are interested in the future of their children do not breed recklessly. The countries in which the care of children is most emphasized are not those with an excessive birth rate, nor do they breed weaklings, mental or physical.

All over the world the medical authorities have been dazzled by the ease and by the results of mass methods of prevention and by the heroics of therapeutic miracle. It is urgently necessary for the leaders of medicine to cultivate that rare and most necessary factor, common sense, and to decide, with McCollum, that society must measure its well-being in terms of the health of its children.

COUNCIL ON PHYSICAL MEDICINE AND REHABILITATION

REPORT OF THE COUNCIL

The Council has authorized publication of the following article.

RALPH E. DE FOREST, M.D., *Secretary.*

INTRACERVICAL AND INTRAUTERINE DEVICES

Some contraceptive methods are not health hazards, whereas others endanger the well-being and health of their users. The booklet, "Apparatus Accepted by the Council on Physical Medicine and Rehabilitation," lists diaphragms and sheaths. When these products are used correctly, the evidence available indicates that they are not health hazards.

In general, intracervical and intrauterine devices are hazardous to the user. These devices are of various shapes and styles, but all have in common a cap that is held over the os uteri externum by a stem that flares in one way or another within the uterus to hold the pessary in place. Pessaries can have a legitimate use and can be highly effective for therapeutic purposes as a means for obtaining drainage, when conditions so indicate.

There can be little doubt, however, that these devices are promoted by some firms primarily for the prevention of conception. One such device has a stem with three conical enlargements aligned so that their apexes point into the uterus. At one end are two prongs and at the other end is a soft rubber button about the size of a nickel. The entire pessary is covered with a coating of rubber. The advertising does not state directly that the pessary is used for contraception. To circumvent this direct claim, the advertising is subtly worded to imply such use, as for example:

> The valvelike action of the cones impedes the progress of flagellate organisms. These organisms become exhausted, their vitality is lowered, their motility reduced and they perish.
>
> The cones, by exerting a gentle pressure upon and by being in constant contact with the ciliated epithelial lining of the cervical canal, interrupt the normal wavelike motion which sweeps inward, thus again impeding the advance of organisms which depend upon this ciliary motion for progress.

Another firm's illustrated catalogue of items for planned parenthood includes diaphragms, contraceptive jellies and creams, diaphragm inserters, and fitting rings and devotes one-half of a page to describing a pessary very similar to the one just described.

The use of stem pessaries has been discontinued by most physicians because of the danger of uterine injury and pelvic infection. Nevertheless, there still appear to be some champions for the contraceptive use of these devices. Although the evidence is not conclusive to indicate that carcinoma has been developed through the use of these devices, the evidence is quite clear to show that uterine and cervical infections may be traced to their use. Pelvic inflammatory diseases and abscesses have necessitated surgical intervention. The metal cervix pessaries have caused endometritis and obstruction to drainage resulting in widespread pelvic infection. Cellulitis may develop from a lost stem which frequently works its way farther upward into the uterus and produces a foreign body reaction. Furthermore, stems may perforate the uterine wall or uterine blood vessels and become embedded so as to create a pathway for the ascent of bacteria into the uterus. Pregnancy may occur in the presence of an intracervical pessary, and if the device remains in place longer than one month, it is likely to cause abortion.

The Council on Physical Medicine and Rehabilitation condemns the use of these devices as a method of achieving contraception because of the lack of evidence to indicate that the device is "nonirritating," "noninjurious," or causes "no troublesome after-effects."

APPARATUS ACCEPTED

The following additional product has been accepted as conforming to the rules of the Council on Physical Medicine and Rehabilitation of the American Medical Association for inclusion in Apparatus Accepted. A copy of the rules on which the Council bases its action will be sent on application.

RALPH E. DE FOREST, M.D., *Secretary.*

Ace Elastic Hose (for Men)

Becton, Dickinson and Company, Rutherford, N. J.

The Ace Elastic Hose (for Men) resemble dress socks and extend to a level just below the knee. They are made of nylon-covered rubber and have complete feet. The weave is described as a two-way stretch. The toe is made of nylon only (no rubber) and the heel of double thread nylon-covered rubber to provide elasticity. The cuff or self-gartering portion of the stocking is made of nylon-covered rubber, double thickness, and has a minimum width of 5 cm. (2 in.) to prevent binding. For the realization of the intended beneficial effects, a proper fit is essential, especially since too tight a fit at the upper end of the stocking will impede venous return flow. Since this stocking ends below the knee, its usefulness in persons with varicose veins is limited to lesions below that level.

Ace Elastic Hose (for Men)

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SURVEY OF PHYSICIAN ATTITUDES

The Council on Medical Service, through its Committee on Prepayment Medical and Hospital Service, is now conducting a survey of physician attitudes concerning voluntary health insurance. With voluntary insurance programs of many types insuring increasing numbers of persons, the attitude of physicians is most important to its continued growth and success. It is the physician who certifies whether a person is disabled and thereby eligible to receive insurance benefits. The physician is also the one who certifies when the patient recovers, when he returns to work, and when he ceases to receive those benefits. In the realm of hospital, surgical, and medical expense benefits the physician is again the one who certifies the need for hospitalization, surgery, etc. In addition, the physician derives a substantial source of his personal income by virtue of insurance benefits that assist insured patients in financing their health care.

There is no uncertainty about the attitude of the vast majority of practicing physicians concerning the relative merits of the many forms of voluntary health insurance over any compulsory tax scheme. Likewise, there is little doubt relative to the opinions of spokesmen for certain nonmedical and noninsurance groups concerning their attitudes about what voluntary insurance can and should accomplish. Insurance, like medicine, is an exacting science and can accomplish only that which comes within the scope of its natural limitations.

Many questionnaires and many opinion surveys have been designed since the advent of health insurance. None, apparently, has attempted to gather information that would indicate the attitude of physicians concerning certain aspects of voluntary health insurance. This is the purpose of the current survey. The Bureau of Medical Economic Research is mailing the questionnaire to avoid the possibility of having the same physicians receive more than one type of questionnaire currently emanating from American Medical Association headquarters.

Health insurance, at times, is subjective. It has created a vocabulary comparatively new to many who have been interested in the topic. The same terms and phrases convey different meanings to different persons according to their own experiences or to the sources of their information. Considerable care has been taken in preparing the current questionnaire to minimize misinterpretations and maximize the accuracy of tabulating opinions in a difficult field. Among other things it is necessary to know to what extent insurance plans may affect the traditionally confidential relationship between the patient and the physician. The survey is also designed to learn how physicians feel about the extent to which insurance involves them in the realm of service benefits and in their financial relationships with patients and how they feel toward the different types of generally available insurance plans.

Although the survey is sponsored by the Council on Medical Service through its Committee on Prepayment Medical and Hospital Service, the questionnaire itself was prepared after deliberations with the Bureau of Medical Economic Research and consultations with a Committee from Blue Shield Medical Care Plans and other groups. The success of any survey is contingent on an adequate sampling coupled with sufficient returns from which to draw reliable conclusions. For the most part, the questionnaire is designed to facilitate completion with a minimum of time and effort. It is to the advantage of the physicians who receive these questionnaires mailed on a random sampling to study them carefully, complete them to the best of their ability, and return them promptly. In this way they will be more properly represented in committee and national conferences involving health insurance.

BLEEDING ESOPHAGEAL VARICES

Esophageal varices develop secondarily to partial or complete obstruction of the portal blood flow at the junction of the esophagus and cardia of the stomach between the coronary vein, a branch of the portal circulation, and the esophageal veins, branches of the azygos vein of the systemic circulation. Portal hypertension may be one of two types, intrahepatic or extrahepatic, or a combination of both. A high retention of sulfobromophthalein in the blood 30 minutes after intravenous injection, a positive reaction to the hippuric acid test, and reversal of the albumin-globulin ratio all point to the diagnosis of cirrhosis of the liver with intrahepatic portal block. In the absence of these findings, one can assume that the block is extrahepatic. Intrahepatic block may be caused by portal cirrhosis of the Laennec type or by thrombosis of the hepatic veins, the so-called Chiari syndrome. The extrahepatic block may be congenital or the result of thrombosis of the portal vein or of one or more of its tributaries. A combination of the two main types may occur. The syndrome of extrahepatic portal bed block described by Banti is characterized by secondary anemia, leukopenia, splenomegaly, and a tendency to repeated massive gastrointestinal hemorrhages, most frequently associated with ruptured esophageal varices.

Exsanguination from bleeding esophageal varices is a frequent cause of death, particularly in portal hypertension with cirrhosis of the liver. Apparently the portacaval shunt created by the natural anastomosis of the two systems at the gastroesophageal junction is inadequate to prevent increased intraportal tension and development of esophageal varices.

Most workers in this field felt that the definitive treatment of bleeding esophageal varices should be one capable of permanently lowering the tension in the portal system. To accomplish this end, attempts were made to establish a portacaval shunt either by anastomosis of the

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portal vein to the vena cava or by an end-to-side anastomosis of the splenic to the renal vein. The idea of shunting portal blood into a systemic vein was conceived by Eck, a young Russian doctor, working in Pavlov's laboratory in 1877. He performed successfully an anastomosis between the portal vein and the vena cava in a dog. The recent interest in portacaval shunts in the treatment of portacaval hypertension in human beings has resulted at least partially from the nonsuture method for blood vessel anastomosis devised by Blakemore and Lord.[1] The shunt procedures, however, are too formidable to be safely performed at the time of an acute hemorrhage. A number of methods were therefore attempted to treat the acute massive hemorrhage caused by a ruptured esophageal varix. Among these were ligation of the splenic artery, ligation of the splenic and hepatic arteries, injection of the esophageal varices with sclerosing solution, esophagogastrectomy, total gastrectomy, and esophageal tamponage.

The method of balloon tamponage to control bleeding esophageal varices was first reported in 1930 by Westphall (as quoted by Linton). Rowntree and associates [2] reported in 1947 successful use of a balloon tamponage in two grave cases of massive bleeding due to esophageal varix. Sengstaken and Blakemore [3] treated successfully 30 patients with acute hematemesis with a nasogastric tube bearing a reinforced balloon. Blakemore [4] recommended leaving the tube-balloon type of tube in the stomach and the esophagus for a week or more, feeding the patient through a third lumen in the tube. The tamponage method, temporarily successful, was not infrequently followed by a recurrence of bleeding after the nasogastric tube was removed. Linton and Warren [5] stress that in patients with signs of impending hemorrhagic shock immediate balloon tamponage should be performed and this should be followed, as soon as the hemorrhage is controlled, by an emergency operation consisting of a transesophageal suture of the varices.

Crile [6] in 1950 reported on seven patients with severe recurring bleeding whom he successfully treated by transesophageal ligation of the varices. He regarded this procedure as a definitive operation rather than one to control the bleeding only at the time of hemorrhage. Linton and Warren,[5] however considered it as a lifesaving procedure at the time of acute hemorrhage but not as a definitive treatment of esophageal varices. They believed that this could be accomplished only by the formation of some portacaval shunt. The time interval between the two procedures, it was felt, should allow for maximum improvement in the underlying liver cirrhosis.

The rationale of the portacaval shunt for the relief of portal hypertension, as pointed out by Blakemore,[4] has been adequately corroborated by portal pressure measurements made at the time of the operation before and after the establishment of shunts. The establishment of an anastomosis of the portal vein to the vena cava or the splenic vein anastomosed end to side with the left renal vein following splenectomy creates a shunt with a low resistance to blood flow. Under these circumstances a large volume of blood will pass from the relatively high pressure portal system directly into the low pressure caval system via the shunt. This results in a marked reduction of the portal pressure. Linton [7] reported on 77 patients who survived the formation of a portacaval shunt; 8 of these patients (10.7%) are now dead and the remaining 69 (90%) are alive and for the most part in good health. Blakemore [4] reported an over-all operative mortality of 17.8% for a series of 140 cases.

Factors influencing operative risk are those of the functional status of the liver and the deleterious effects on the liver of the long-standing portal hypertension. The improvement in the operative results in the last few years is due to advances in the medical treatment of cirrhosis of the liver and the knowledge that a cirrhotic liver fortified with proteins, carbohydrates, and vitamins, if protected against anoxia, is far more resistant to decompensation following surgery than a liver not so supported. The availability of whole blood, plasma, and human albumin for the correction of anemia, restoration of blood volume, restitution of depleted proteins, achievement of potential control of infection, and control of blood clotting all, according to Blakemore,[4] are important factors favoring success with venous shunt procedures.

GASTRODUODENAL HEMORRHAGE

Rappaport [1] has brought into focus a perplexing problem in a way that should benefit many future patients with gastroduodenal hemorrhage. Although in some cases the source of the hemorrhage cannot be found, he is specially concerned with that group in whom lesions presumed to be the cause of the hemorrhage are detected by roentgenogram or gastroscopy and in whom at operation the surgeon is unable by palpation and inspection to detect any lesion. He presents five such case reports of patients in whom a first operation failed to reveal the suspected lesion and a second operation was necessitated by a persistence of symptoms. In two of these cases an adenocarcinoma was found. One patient died three months later and the other recovered and had no recurrence of the hemorrhage. One other patient was found to have a lymphosarcoma and died two years after the second operation. The two remaining patients, one with a lipofibroma and one with a duodenal ulcer, recovered and had no recurrence of hemorrhage. Rappaport concluded that palpation and inspection of the stomach at operation may be unreliable and that when there is strong roentgenologic or gastroscopic evidence of a lesion the surgeon should make a greater effort to substantiate these findings, by opening the stomach if necessary.

1. Blakemore, A. H., and Lord, J. W., Jr.: The Technic of Using Vitallium Tubes in Establishing Portacaval Shunts for Portal Hypertension, Ann. Surg. **122**: 476-489 (Oct.) 1945.

2. Rowntree, L. G.; Zimmerman, E. F.; Todd, M. H., and Ajac, J.: Intraesophageal Venous Tamponage: Its Use in a Case of Varical Hemorrhage from the Esophagus, J. A. M. A. **135**: 630-631 (Nov. 8) 1947.

3. Sengstaken, R. W., and Blakemore, A. H.: Balloon Tamponage for the Control of Hemorrhage from Esophageal Varices, Ann. Surg. **131**: 781-789 (May) 1950.

4. Blakemore, A. H.: The Portacaval Shunt for Portal Hypertension with Special Reference to Cirrhosis of the Liver, Bull. New York Acad. Med. **27**: 477-494 (Aug.) 1951.

5. Linton, R. R., and Warren, R.: The Emergency Treatment of Massive Bleeding from Esophageal Varices by Transesophageal Suture of These Vessels at the Time of Acute Hemorrhage, Surgery **33**: 243-255 (Feb.) 1953.

6. Crile, G., Jr.: Transesophageal Ligation of Bleeding Esophageal Varices: A Preliminary Report of Seven Cases, Arch. Surg. **61**: 654-660 (Oct.) 1950.

7. Linton, R. R.: Bleeding Esophageal Varices and Their Surgical Treatment, Maryland State M. J. **2**: 400-411 (Aug.) 1953.

1. Rappaport, E. M.: Gastroduodenal Hemorrhage: Difficulties in Recognition of Lesions at Operation by Palpation and Inspection, Ann. Int. Med. **39**: 747-756 (Oct.) 1953.

MEDICAL NEWS

CALIFORNIA

Symposium on Infectious Diseases.—The California Academy of General Practice in conjunction with Lederle Laboratories will present on Dec. 9 at 10 a. m. a symposium on acute infectious diseases at the Hotel Del Coronado, Coronado. Luncheon will be served. There will be no registration fee.

Pathologists Meet in San Francisco.—The California Society of Pathologists will hold its annual meeting at the Fairmont Hotel, San Francisco, Dec. 5-6. The program, under the auspices of the California Society of Pathologists, the southwestern region of the College of American Pathologists, and the Cancer Commission, will include papers on trace metals and hepatic clearance, a panel on chromatography, and a tumor slide conference.

School Celebrates Anniversary.—The 25th anniversary of the University of Southern California School of Medicine, Los Angeles, was celebrated with a banquet and a convocation on phases of medical education and research, Sept. 24-25. At a dinner at the Ambassador Hotel, Dr. Alan Gregg, medical director of the Rockefeller Foundation in New York, gave an address. At a convocation at the Los Angeles County Hospital, Dr. Paul D. White, Boston, Dr. Hugh J. Morgan, Memphis, and Dr. Arthur L. Bloomfield, San Francisco, were the speakers on whom honorary degrees were conferred for outstanding service in the field of medicine.

CONNECTICUT

Geriatric Study.—Meriden has been selected as the site for an intensive study of the potentials of the aging, according to an announcement by the chairman of the commission to study the potentials of the aging, appointed by Gov. John D. Lodge last July. The final report is to be made on or before July 1, 1954.

Personal.—Dr. Thomas P. Murdock, Meriden, has accepted appointment by Gov. John D. Lodge as the physician member of the state commission, authorized by the 1953 General Assembly, to study the possibilities of the development of a regional professional school including medicine.——Dr. Norman L. Cressy has been appointed director of medical education at Uncas-on-Thames, state tuberculosis sanatorium, Norwich. Dr. Cressy served on the Respiratory Disease Commission, U. S. Army, during World War II, and was previously instructor in medicine, Yale University School of Medicine, New Haven.——Dr. Albert S. Gray, who retired July 1 as deputy commissioner of the Connecticut State Department of Health, has been honored with life membership in the Connecticut Safety Society. The award was presented during the society's meeting on Sept. 28 by Everett W. Martin, past president.

DELAWARE

State Medical Election.—At the annual meeting in Wilmington, the Medical Society of Delaware elected Dr. Hewitt W. Smith, Harrington, president, Dr. Lewis B. Flinn, Wilmington, president-elect, Dr. Glenn W. M. Van Valkenburgh, Georgetown, vice-president, Dr. Norman L. Cannon, Wilmington, secretary, and Dr. Charles Levy, Wilmington, treasurer.

Personal.—A citation was presented to Dr. George H. Gehrmann, Wilmington, medical director of the DuPont Company, by the Malvern (Pa.) Institute for Alcoholism and Psychiatric Studies, in recognition of "the exemplary leadership and courage he has displayed in furthering the treatment, understanding, and welfare of the alcoholic patient and for many years of outstanding service in this cause."

Meeting on General Practice.—The Delaware Academy of General Practice will hold its annual scientific session on Dec. 12 at the Delaware Academy of Medicine in Wilmington. At 10 a. m. Dr. Herman K. Hellerstein, Western Reserve University School of Medicine, Cleveland, will deliver the William J. Urie, M.D., memorial lecture, "The Rehabilitation of the Cardiac," sponsored by Wyeth, Philadelphia. The following program will then be presented:

Drugs and Procedures in Treatment of Peripheral Vascular Diseases, Meyer Naide, Woman's Medical College of Pennsylvania, Philadelphia.
Pathophysiology and Treatment of Congestive Heart Failure, Thomas M. Durant, Temple University School of Medicine, Philadelphia.
Useful Medications in Gastroenterology, James L. A. Roth, Graduate Hospital of the University of Pennsylvania, Philadelphia.
The Electroenterogram, A. Lee Lichtman, New York Polyclinic Medical School and Hospital, New York.
Parenteral Carbohydrate Therapy in Medicine, Jacob J. Weinstein, George Washington University School of Medicine, Washington, D. C.
The Management of Pain, Donald H. Stubbs, George Washington University School of Medicine, Washington, D. C.
The General Practitioner as a Urologist, Elmer Hess, Erie, Pa.

At 7 p. m. the annual banquet and dance will be given at the Brandywine Country Club. The guest speaker, Dr. John S. DeTar, Milan, Mich., speaker of the house of delegates, American Academy of General Practice, will discuss "The General Physician and His Problems."

FLORIDA

Society News.—The Florida Pediatric Society has elected Dr. C. Jennings Derrick, West Palm Beach, president, and Dr. Wesley S. Nock, Coral Gables, secretary-treasurer.

Narcotic Violation.—Dr. James Ryan Chandler Sr., Daytona Beach, pleaded guilty in U. S. District Court at Jacksonville to violation of the federal laws relating to the illegal use of narcotics (USC Title 18, Section 494) and on Aug. 21 was sentenced to serve a term of two years.

Otologic-Ophthalmologic Seminar.—The eighth annual University of Florida Midwinter Seminar in Ophthalmology and Otolaryngology will be held at the Sans Souci Hotel, Miami Beach, the week of Jan. 18, 1954, lectures on ophthalmology being presented Jan. 18-20 and on otolaryngology, Jan. 21-23. A midweek feature will be the Midwinter Convention of the Florida Society of Ophthalmology and Otolaryngology, Jan. 20, to which all registrants are invited. The registrants and their wives may also attend the informal banquet at 8 p. m. Wednesday. The seminar schedule permits ample time for recreation. Lecturers on ophthalmology will be Drs. William B. Anderson, Durham, N. C., William P. Beetham, Boston, William C. Owens, Baltimore, Algernon B. Reese and Maynard C. Wheeler, New York; lecturers in otolaryngology, Drs. Edwin N. Broyles, Baltimore, Howard P. House, Los Angeles, William J. McNally, Montreal, Canada, Dorothy Wolff, Ph.D., and Dr. Degroff Woodman, New York.

ILLINOIS

Fellowships in Statistics.—Three $4,000 postdoctoral fellowships in statistics are offered for 1954-1955 by the University of Chicago to holders of the doctor's degree or its equivalent in research accomplishment. The purpose of these fellowships is to acquaint established research workers in the biological, physical, and social sciences with the role of modern statistical analysis in the planning of experiments and other investigative programs and in evaluation of empirical data. The closing date for applications is Feb. 15, 1954; instructions for applying may be obtained from the Committee on Statistics, University of Chicago, Chicago 37.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education and public health. Programs should be received at least three weeks before the date of meeting.

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Chicago

Dr. White to Lecture on Rheumatic Fever.—The first annual Harry G. Remer lecture on rheumatic fever will be delivered by Dr. Paul D. White, Boston, Dec. 11, 8 p. m., at La Rabida Sanitarium. This lecture is open to the public and is free.

Dr. Baker Appointed Professor of Urology.—Dr. Roger C. Baker Jr., associate professor of urology, University of Chicago School of Medicine and the Albert Merritt Billings Hospital, has been appointed professor of urology at the Georgetown University School of Medicine, Washington, D. C. Dr. Baker has engaged in work in urology also at the U. S. Naval Hospital in Philadelphia and the Massachusetts Memorial Hospitals in Boston. In 1950 he received the annual research award of the American Urological Association.

Medical Stamps.—At the annual exhibit of the Philatelic Society in Chicago, Dec. 3-5, Miss Margaret M. Bates, medical sciences librarian, University of Illinois, is exhibiting 54 pages of stamps depicting medical and scientific achievements from mythology and from Greek, Arabic, and Egyptian medicine and the subsequent primitive witch doctor, to the era of scientific specialization. Physicians who were statesmen, presidents of their countries, and explorers, others honored for their medical achievements, and cancer, leprosy, bacteriology, pathology, medicine, child welfare, and medical congresses are among the subjects.

Personal.—Dr. August F. Daro was elected chairman of the obstetric and gynecologic section of the International College of Surgeons at the annual meeting in New York.——Richard J. Winzler, Ph.D., professor and head of the department of biochemistry, University of Illinois College of Medicine, has been named consultant to the department of biochemistry of Cook County Hospital and the Hektoen Institute for Medical Research.——Dr. Ulysses G. Dailey, past president of the National Medical Association and former editor of its journal, has returned from a second tour of foreign countries under the auspices of the U. S. Department of State, as "leader-specialist" of the U. S. Information and Educational Service. Dr. Dailey delivered addresses at the All-Pakistan Medical Conference in Lahore, the India Medical College in Gwalior, the University of Ceylon, and numerous meetings of medical associations and special groups in Pakistan, India, Ceylon, and Africa.

IOWA

Society News.—Leslie M. FitzGerald, D.D.S., Dubuque, president-elect of the American Dental Association, was recently honored by the Dubuque County Medical Society at a banquet and program in the Hotel Julien, Dubuque. Officers of the American Dental Association and the Iowa State Dental Society were guests, together with the Dubuque County Dental Society and many dentists from Iowa, Illinois, and Wisconsin.

MICHIGAN

Lecture on Arthritis.—The Wayne County Medical Society, Detroit, will have as its speaker, Dec. 7, Dr. Otto Steinbrocker, New York, who will discuss "Treatment of Arthritis."

Edsel B. Ford Lecture.—On Dec. 8, at 8:15 p. m. in Henry Ford Hospital auditorium, James Hillier, Ph.D., research physicist, R.C.A. Laboratories, Princeton, N. J., will present the Edsel B. Ford lecture, "Some Results of the Application of Electron-Microscopy to Medicine."

Medicolegal Institute.—This institute, under the sponsorship of the State Bar of Michigan, will be held at the Sheraton-Cadillac Hotel, Detroit, Dec. 10-11. This will be the first "integral short course" of an over-all "three interval course," each to follow at an approximate six month period. Members of the Michigan State Medical Society are cordially invited. Advance registrations may be made by sending $25, payable to the Michigan Law Institute, % State Bar of Michigan, 412 Olds Tower Bldg., Lansing.

MISSOURI

Lecture on Gout.—Dr. Alexander B. Gutman, professor of medicine, Columbia University College of Physicians and Surgeons, New York, will speak in the Auditorium of Kansas City Municipal Hospital No. 1 on Dec. 17 at 8 p. m. His subject will be "Gout."

Society News.—The St. Louis Society of Neurology and Psychiatry will have as guest speaker on Dec. 10 at 8:15 p. m. Dr. Henry A. Davidson of the Veterans Administration Central Office, Washington, D. C., who will present "Role of the Psychiatrist in the Administration of Criminal Justice." Discussion will be by Dr. Val B. Satterfield of St. Louis. The meeting will be held in Elliott Auditorium of McMillan Hospital, St. Louis.

Personal.—Dr. Julius Jensen, St. Louis, has received the Distinguished Service award given annually by the American Medical Writers' Association to a member of the association, "who has made distinguished contributions to medical literature or rendered unusual and distinguished service to the medical profession." Dr. Jensen is president-elect of the Missouri Heart Association, a former professor at Washington University School of Medicine, and the author of books and scientific articles.

NEW JERSEY

Joint Meeting for Martland Lecture.—The Essex County Pathological and Anatomical Society will meet with the Academy of Medicine of New Jersey and the Essex County Medical Society, Dec. 9, 9 p. m., at the Academy of Medicine, 91 Lincoln Park, Newark, to hear Dr. Paul Klemperer, pathologist to Mount Sinai Hospital and professor of pathology, Columbia University College of Physicians and Surgeons, New York, deliver the Harrison S. Martland lecture. A dinner will precede the meeting.

Tumor Slide Seminar.—The New Jersey Society of Clinical Pathologists will hold its annual slide seminar on unusual tumors at the Nurses' Auditorium of Presbyterian Hospital, Newark, Dec. 12, 2 p. m. Drs. Fred W. Stewart and Frank W. Foote Jr. of the Memorial Center for Cancer and Allied Diseases, New York, will act as moderators. Slides and case histories prepared by the Bureau of Pathology, New Jersey State Department of Health, are being sent to all members of the state society of pathologists. Voting on the slides will be analyzed by Drs. Stewart and Foote at the meeting. Visitors to the seminar will be welcome.

General Practitioners Meet in Newark.—The New Jersey Academy of General Practice will hold its annual scientific session Dec. 9 at the Hotel Essex House, Newark. "Office Diagnosis and Treatment of Upper Gastrointestinal Disturbances" will be developed in the following program:

Moses Paulson, Baltimore, Practical Consideration of Functional Disorders of the Stomach.
Eddy D. Palmer, Washington, D. C., Specific and Nonspecific Gastric Inflammation, Using Office Methods for Diagnosis.
Emmanuel Deutsch, Boston, Gastric Cancer.
Sara M. Jordan, Boston, Treatment of Peptic Ulcer with Special Emphasis on the Use of the Newer Drugs.

All physicians are invited. There is no registration fee.

NEW YORK

Hospital News.—The Jewish Sanitarium and Hospital for Chronic Diseases, Brooklyn, will present "Urologic Complications in Gynecology" by Dr. Houston S. Everett, associate professor of gynecology, Johns Hopkins University School of Medicine, Baltimore, Dec. 10, 8:30 p. m., in the auditorium. Dr. Everett is the author of "Gynecological and Obstetrical Urology." Medical guests are cordially invited.

Meeting on Circulatory Diseases.—The New York Society for Circulatory Diseases will devote its regular meeting, 8:30 p. m., Dec. 8, in the New York Academy of Medicine building, to consideration of treatment of acute cardiac emergencies in myocardial infarction. Dr. Maurice L. Tainter, director, Sterling-Winthrop Research Institute, Rensselaer, will speak

on shock, and Dr. Herbert J. Kayden, clinical instructor in medicine, New York University College of Medicine, will discuss "Paroxysmal Arrhythmias and Heart Block."

Appointments at Brookhaven Laboratory.—Recent appointments to the medical department of Brookhaven National Laboratory, Upton, include: Drs. George C. Cotzias and Bernard G. Stall III, each formerly assistant to the institute and assistant to the hospital at the Rockefeller Institute for Medical Research, New York; Dr. Charles G. Lewallen, Cleveland, formerly at the U. S. Naval Hospital, St. Albans; Dr. Edward T. Dunham; Dr. Laurence S. Maynard, Rinerhead, N. Y., previously deputy commissioner of the Suffolk County Department of Health; and Dr. Hadley L. Conn Jr., Philadelphia.

Pilot Rehabilitation Project.—The diagnostic and evaluation division of the Queens Rehabilitation Program, a pilot project for handicapped children for other communities of the nation, was dedicated on Nov. 10 at Queens General Hospital, 164th St. and Grand Central Parkway, Jamaica. The division's rehabilitation program grew out of two years' planning by representatives of 20 health, welfare, civic, and business groups working with the Association for the Aid of Crippled Children. The program will seek out all Queens children who need help, correct the handicapping condition as far as possible, help the children to develop healthy attitudes, promote a better understanding of the handicapped, provide training opportunities, and stimulate research in methods of prevention, early discovery, and proper care of handicapping conditions.

Buffalo Dedicates Capen Hall.—The University of Buffalo schools of medicine and dentistry on Dec. 11-12 will dedicate Samuel P. Capen Hall, a building recently completed at a cost of $4,500,000 and named for the chancellor emeritus of the university, who will be guest of honor. Friday morning the following symposium will be presented:

The University and the Community, J. Roscoe Miller, Northwestern University, Evanston, Ill.
The Heritage of William Osler in 1953, Stanley E. Dorst, University of Cincinnati College of Medicine.
Trends in Dental Education, Maynard K. Hine, D.D.S., Indiana University School of Dentistry, Indianapolis.
The Cornerstone: Samuel P. Capen, Mr. John M. Russell, New York, John and Mary R. Markle Foundation.

Friday afternoon Dr. Stockton Kimball, dean, University of Buffalo School of Medicine, will preside at a conference on structural and immunological basis of biological specificity, during which Dr. Ernest Witebsky, professor of bacteriology and immunology, will discuss "Immunological Aspects of Biological Specificity." Robin R. A. Coombs, Ph.D., assistant director of research, department of pathology, University of Cambridge, England, will present "Immunology and the Natural Sciences." At 9:30 a. m. Saturday, Dr. Charles H. Best, director, Banting-Best Institute, University of Toronto, Canada, will preside at the following medical conference:

Fat in Parenteral Nutrition, Fredrick J. Stare, Harvard School of Public Health, Boston.
Amino Acids in Parenteral Nutrition, Herbert Pollack, Columbia University College of Physicians and Surgeons, New York.
Parameters of Electrolyte Needs During Parenteral Nutrition, Thaddeus S. Danowski, University of Pittsburgh School of Medicine.
Metabolic Consequences of Stress in Man, Jerome W. Conn, University of Michigan Medical School, Ann Arbor.
The Diet and the Cholesterol Problem, Ancel B. Keys, Ph.D., University of Minnesota Medical School, Minneapolis.

During the dental conference, which will be held simultaneously, Dr. William F. Harrigan, New York University College of Dentistry, will consider "Diagnosis in the Field of Oral Surgery." At the general alumni luncheon in the Clark Memorial Gymnasium, 12:30 p. m., Dr. Charles Gordon Heyd, New York, past president of the American Medical Association, will discuss "The Place of a Private University in Our Society." On Sunday the hall will be open to the public from 2 to 6 p. m.

New York City

Dr. Lewis to Head Neuropsychiatric Institute.—Dr. Nolan D. C. Lewis, director of the New York State Psychiatric Institute since June, 1936, has retired from that position to devote full time to his new work as director of research in neurology and psychiatry of New Jersey hospitals and agencies. His headquarters are at the Neuropsychiatric Institute, Skillman, N. J., formerly known as the State Village for Epileptics. He will continue his work as managing editor of the *Journal of Nervous and Mental Disease*, the *Psychoanalytic Quarterly*, and the *Journal of Child Behavior*.

Courses in Accident Prevention.—The Center for Safety Education, New York University, will offer courses in industrial and traffic accident prevention during the spring term, which begins Feb. 1, 1954. Courses will include: Safety Directors and Safety Engineers—Their Qualifications, Duties, and Responsibilities; Safety Organization: Values and Limitations; Management and Supervision in Accident Prevention; Industrial Hygiene and Occupational Diseases; Accident Prevention for Operators of Smaller Motor-Vehicle Fleets: Operating the Program; Special Problems in Accident Prevention; Psychology of Accident Prevention; Accident Prevention for Small Firms; and Marine Accident Prevention. Information may be secured from the Center for Safety Education, New York University, Washington Square, New York 3.

Assembly in Anesthesiology.—The New York State Society of Anesthesiologists will hold its seventh postgraduate assembly in anesthesiology, Hotel New Yorker, Dec. 9-12. Topics for discussion include the neuromuscular junction, hospital hazards, artificial support of circulation, adrenal mechanisms pertinent to anesthesiology, physiology and pharmacology of hypotension, applied pharmacology and mechanisms of action of barbiturates, local anesthesia, and neonatal survival. "Lunch with the Experts," round-table discussions, will be held Thursday and Friday. Saturday will be devoted to a residents' program. There will be a dinner dance Thursday, and Friday Dr. Louis H. Bauer, Hempstead, Immediate Past President of the American Medical Association, will be guest speaker at dinner. He will present "Current Medical Problems Affecting the Anesthesiologists."

Leukemia Award.—The Robert Roesler de Villiers award was conferred on Dr. Ludwik Gross, Oct. 20, for his contributions to the knowledge of the nature and cause of leukemia. The award was presented at ceremonies at the New York Academy of Medicine, in which Dr. Maxwell M. Wintrobe, University of Utah School of Medicine, Salt Lake City, and Dr. William B. Castle, Harvard Medical School, Boston, spoke about leukemia research. Dr. Gross, who is chief of research at the Veterans Administration Hospital, New York, was associated with the Pasteur Institute in Paris for seven years and received the Chevillon prize of the Academy of Medicine in Paris in 1937. The Robert Roesler de Villiers Foundation was created in 1949 in memory of a youth who died of leukemia. Through periodic international contests the foundation offers awards to researchers all over the world for development toward the prevention, effective treatment, or cure of leukemia. Members of the jury, in addition to Drs. Wintrobe and Castle, are Dr. Albert Alder, University of Zurich, Switzerland, and Dr. Jan Waldenstroem, University of Lund, Malmoe, Sweden. In this, the second contest, 226 papers were submitted from 22 countries in six languages. The foundation will support, financially or otherwise, studies of theories or therapies which the jury considers of potential value. It also will assist needy leukemia patients. The foundation is not endowed and depends entirely on voluntary contributions, which are tax exempt.

Personal.—Dr. Samuel Rosen, associate otologist at the Mount Sinai Hospital, has gone to Tel Aviv at the invitation of the Israeli government to work in the new audiology center and to teach surgical treatment of Ménière's disease and otosclerosis.——Dr. Jerome L. Leon, former supervisor of Riverside Hospital's narcotics treatment division, has been named medical director and superintendent of the Sanatorium of the Jewish Consumptives' Relief Society at Spivak, Colo. He succeeds Dr. William S. Klein, who has taken a position with the Veterans Administration in Albuquerque, N. Mex.——Dr. Madison Baldwin Brown, member of the board of directors of the Hospital Council of Greater New York, has been

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appointed medical director of Hahnemann Hospital, Philadelphia, to succeed Dr. Raymond S. Leopold, retired. Dr. Brown has served as medical director of Roosevelt Hospital, assistant professor of hospital administration at Johns Hopkins Hospital, Baltimore, and as a staff member of Columbia University College of Physicians and Surgeons.——Dr. W. Lynwood Heaver has been appointed medical director of the National Hospital for Speech Disorders, 61 Irving Place.——Dr. Donald B. Armstrong, second vice-president of the Metropolitan Life Insurance Company, will retire as head of the health and welfare division on Dec. 31 and will be succeeded by Dr. William P. Shepard of the company's Pacific Coast head office in San Francisco, who recently was transferred to New York. Dr. Shepard has served on the A. M. A. Council on Industrial Health and as president of the American Public Health Association.

OHIO

Society News.—Dr. Hayes Martin, New York, will discuss "Diagnostic Significance of a Lump in the Neck" before the Fort Steuben Academy of Medicine, meeting in the Fort Steuben Hotel, Steubenville, Dec. 8. Physicians, interns, and graduate nurses are invited. Information may be obtained from Dr. Edward B. Weinman, secretary-treasurer, National Exchange Bank Building, Steubenville.

Cancer Laboratory to Memorialize Senator Taft.—Judge Alfred K. Nippert, formerly of the Hamilton County Court of Common Pleas, has announced a gift of $100,000 toward the creation of a cancer research laboratory in memory of the late Sen. Robert A. Taft as part of the Christ Hospital Institute of Medical Research, Cincinnati. Judge Nippert, chairman of the board of Christ Hospital, last year gave $400,000 toward erection of the new medical research building at this hospital.

PENNSYLVANIA

Society News.—On Dec. 15 the Allegheny County Medical Society, 225 Jenkins Bldg., Pittsburgh, will hold a joint meeting with the Western Pennsylvania Heart Association. Dr. Wright R. Adams, professor of medicine, University of Chicago School of Medicine, will discuss "Pulmonary Hypertension."

Appoint Director of Child Guidance Center.—Dr. William F. Finzer, director of the Guidance Institute of Berks County at Reading for the past five years, has been named director of the Pittsburgh Child Guidance Center at the University of Pittsburgh Medical Center. He will also be an assistant professor of psychiatry in child development at the University of Pittsburgh School of Medicine. Dr. Finzer practiced psychiatry at the Menninger Clinic, Topeka, Kan., 1944-1945 and then for two years was with the U. S. Army, serving as chief of neuropsychiatric service for the Neuropsychiatric Center in Tokyo.

Philadelphia

Dr. Gruber Goes to California.—Dr. Charles M. Gruber, professor of pharmacology, Jefferson Medical College of Philadelphia since 1932, has been named head of the department of pharmacology at the College of Medical Evangelists, Loma Linda, Calif. Dr. Gruber is a past president of the American Society for Experimental Biology and Medicine.

TEXAS

Medical Students' Day in Galveston and Houston.—The Texas Medical Association and the local medical societies will sponsor in Houston and Galveston identical programs, designed to acquaint medical students with the practical aspects of future medical practice. In Houston, the meeting will begin at 4 p. m. on Dec. 11 in the Baylor University College of Medicine auditorium with greetings by Dr. John K. Glen, Houston, president of the Harris County Medical Society. In Galveston, the University of Texas Medical Branch will begin its program at 9:30 a. m. on Dec. 12 in the school auditorium, with greetings by Dr. Jesse B. Johnson Sr., president of the Galveston County Medical Society. On each program will be an address to senior students by Dr. George Turner, El Paso, president of the Texas Medical Association, whose subject will be "Your Responsibility as Doctors." The speakers' panel includes: "Your Practice and Public Opinion" by Dr. Troy A. Shafer, Harlingen, chairman, committee on public relations, Texas Medical Association; "You and the Medical Society" by Dr. Francis J. L. Blasingame, Wharton, member of the A. M. A. Board of Trustees; "The Legal Aspects of Your Practice" by Philip R. Overton, Austin, general counsel of the Texas Medical Association; and "The Business Side of Your Practice" by Dr. Harvey Renger, Hallettsville, chairman, council on medical economics, Texas Medical Association.

WISCONSIN

State Medical Election.—At the recent annual meeting in Milwaukee, the State Medical Society of Wisconsin chose the following new officers: president, Dr. H. Kent Tenney, Madison; president-elect, Dr. Arthur J. McCarey, Green Bay; speaker of the House of Delegates, Dr. Lien O. Simenstad, Osceola; and alternate delegate to the A. M. A., Dr. George E. Forkin, Manasha.

New Paging System.—A new system for public paging of its members has been activated by the Medical Society of Milwaukee County. Each member has been assigned a numbered card, the number to be used by members of his family, his hospital, the Medical Society Physicians' Service, or his office when it is necessary to reach him while he is in a public place or at a public gathering.

Sparta Honors Dr. Beebe.—Residents of Sparta and the surrounding area recently gathered at the courthouse square to pay tribute to Dr. Spencer D. Beebe, who in 1954 will complete 50 years of service to the community. "Dr. Beebe Night" was sponsored by the Sparta Kiwanis Club. Dr. Beebe, a life member and past officer of the Wisconsin State Medical Society, was honored by the society as the Wisconsin country practitioner of 1950.

PUERTO RICO

Annual Meeting in Santurce.—The Puerto Rico Medical Association will hold its annual assembly in the association headquarters, Santurce, Dec. 9-13, under the presidency of Dr. Luis A. Sanjurjo, Santurce. Dr. Charles C. Higgins, Cleveland, will participate Thursday in a symposium on the management of urinary lithiasis. On Saturday there will be a symposium on current research in the basic medical sciences of the School of Medicine. Dr. Rudolph H. Kampmeier, Nashville, who with Dr. Felix M. Reyes, Santurce, will conduct a clinical pathological conference at the Hospital San Patricio on Friday, will discuss "The Variability of Diffuse Arteritis (Collagen Diseases)" on Saturday. Other guests of honor and their first presentations include:

Leo H. Bartemeier, Detroit, Utilization of Psychiatric Principles in the Practice of Medicine.
Vicente Pardo-Castello, Havana, Cuba, Early Diagnosis of Leprosy.
Frederick F. Yonkman, Summit, N. J., Certain Phases of the Modern Medical Treatment of Hypertension.
Joseph C. Yaskin, Philadelphia, Evaluation of Headache from the Standpoint of Diagnosis and Treatment.
George T. Pack, New York, Problems of Pigmented Moles and Malignant Melanoma.
Angel Jorge Echeverri, Santiago de Compostela, Spain, Anatomical Clinic Studies on Dysmorphogenesis of Sacrolumbar Region.

GENERAL

Association of Medical Colleges.—At the recent annual meeting in Atlantic City, the Association of American Medical Colleges broadened its membership base to include individuals and organizations with an interest in medical education. Institutional membership had been limited to accredited medical schools. Membership is now open to medical school faculty members and others professionally linked to medical schools for an annual fee of $10; sustaining membership, at $1,000 a year, may be held by interested organizations. The 65th annual meeting, scheduled for Oct. 17-20, 1954, French

Lick Springs Hotel, French Lick, Ind., will be preceded by the association's Teaching Institute on Pathology, Bacteriology, Immunology and Genetics, Oct. 10-15, and by a meeting of medical school cancer coordinators Oct. 15-16 (*J. A. M. A.* Nov. 14, 1953, p. 1023).

Meeting on Nervous and Mental Disease.—The Association for Research in Nervous and Mental Disease will hold its annual meeting at the Hotel Roosevelt, New York, Dec. 11-12. The chief topics for discussion are "Genetics, Human Inheritance and Environmental Effects" and "Neurological and Mental Patterns and Their Inheritance." Participants in the program include Drs. Albert B. Sabin and Josef Warkany, Cincinnati; Arnold L. Gesell and Milton J. E. Senn, New Haven, Conn.; Tryphena Humphrey, Pittsburgh; C. Nash Herndon, Winston-Salem, N. C.; George A. Jervis, Thiells, N. Y.; F. H. Tyler, Salt Lake City; John W. Schut, Anoka, Minn.; William G. Lennox, Boston; Donald H. Jolly, Wrentham, Mass.; Harold G. Wolff, Bernard D. Davis, and Franz J. Kallmann, New York; Leo Kanner, Baltimore; Robert E. Yoss, and James V. Neel, Ann Arbor, Mich.

Borden Award in Nutrition.—Nominations are solicited for the 1953 award of $1,000 and a gold medal made available by the Borden Company Foundation. The American Institute of Nutrition will make this award in recognition of distinctive research by investigators in the United States and Canada that has emphasized the nutritive significance of the components of milk or of dairy products. The award may be divided between two or more investigators, but employees of the Borden Company are not eligible for the award. Formal presentations will be made at the annual meeting of the institute in the spring of 1954. Nominations, which must be in the hands of the chairman of the nominating committee, J. B. Brown, Ph.D., Institute of Nutrition and Food Technology, Ohio State University, Columbus 10, Ohio, by Jan. 1, 1954, should be accompanied by such data relative to the nominee and his research as will facilitate consideration for the award.

Damon Runyon Cancer Grants.—The Damon Runyon Memorial Fund for Cancer Research allocated $76,500 for the month of October for seven institutional grants and two fellowships to train cancer research investigators. The grants included: $10,000 for a project entitled "The Relationship of Hormones in Neoplasia," to be conducted by Dr. Albert Segaloff at Tulane University of Louisiana Medical School, New Orleans; $20,000 to the Institute for Cancer Research, Inc., Philadelphia, for a projected research study under Dr. Stanley P. Reimann, entitled "Physicochemical Study of Cancer Patients"; and $10,000 to Dr. Harold S. Diehl, dean of medical sciences at the University of Minnesota Medical School, Minneapolis, who heads an investigation on endocrine aspects of malignant growth. To date of report, $7,323,286 had been allocated by the fund in 395 grants and 258 fellowships, in 170 institutions in 47 states, the District of Columbia, and 14 foreign countries.

Booklet for Multiple Sclerosis Patients.—An illustrated booklet "Mental Health and MS," published by the National Multiple Sclerosis Society, 270 Park Ave., New York 17, is available to multiple sclerosis patients, according to an announcement by Dr. Harold R. Wainerdi, New York, medical director of the society. The booklet is the result of a grant made in 1949 by the society to the New York University-Bellevue Medical Center to support a study on the psychological factors in multiple sclerosis, under the direction of Molly Harrower, Ph.D., who is now consultant in psychology, U. S. Army, and research director, Court Intake Project, New York City, Court of Domestic Relations. The booklet contains two vocational interest tests designed to give patients an understanding of their interests and vocational potentialities. The importance of hobbies and creative interests is stressed. The booklet will be distributed without charge to multiple sclerosis patients on request directed to the National Multiple Sclerosis Society or any affiliated chapter of the society. A second mental health booklet by the same author, for use of physicians who treat multiple sclerosis patients, will be published shortly.

Radiologists Meet in Chicago.—The Radiological Society of North America will hold its annual meeting, Dec. 13-18, at the Palmer House, Chicago. Fifty-seven papers are scheduled for presentation, and seven will be read by title. Ninety-two speakers by invitation are listed. A symposium on isotope studies is scheduled for Monday morning. Monday afternoon a chest survey will include "The Value of Chest Surveys from the Standpoint of the Internist," "The Radiologist and Chest Surveys," "The Administrator Looks at Chest Surveys," "Chest Surveys as Used by the Chest Physician," and "What the Public Thinks of Chest Surveys." The radiobiology session will be held Tuesday morning, the radiological physics session Wednesday morning, and the radiobiology and physics session Friday morning. Thursday morning there will be a panel discussion on low back pain and a symposium on radiation units and Thursday afternoon, a symposium on rotation therapy. The annual banquet will be held Thursday, 7 p. m. The Carman lecture, "Observations in Atomic Medicine," by Dr. Roger Allen Harvey, acting dean, University of Illinois College of Medicine, Chicago, will be delivered Tuesday at 8:30 p. m. The society has scheduled 47 refresher courses.

International Cancer Congress.—Physicians are invited to present papers at the sixth International Cancer Congress, to be held in São Paulo, Brazil, July 23-29, 1954, under the sponsorship of the International Union Against Cancer. The program will include sections on fundamental cancer research, clinical studies on cancer, and cancer control. Registration blanks are available from the Chairman, National Committee on International Union Against Cancer, National Research Council, 2101 Constitution Ave. N.W., Washington 25, D. C. Five copies of an abstract of each paper proposed for presentation must be sent to the chairman by Jan. 15, 1954. Abstracts are not to exceed 250 words and must be accompanied by a title and the name, address, academic or professional title, and institutional affiliation of the investigator or physician. These requirements do not apply to persons who have been invited to participate by the president of the congress unless application is made for travel allotments as described below. It is expected that round-trip transportation by air from Miami to São Paulo will be available for about $480. Detailed information regarding travel arrangements and hotel reservations may be obtained from Dr. Brewster S. Miller, American Cancer Society, Inc., 47 Beaver St., New York 4. Travel allotments of approximately $600 each will be available to a limited number of individuals requiring such assistance. Applications for travel allotments must be submitted in quintuplet to the chairman by Jan. 15. They should be in letter form, giving information concerning age, training, publications in cancer or related fields, and academic or professional status. Applicants not planning to present papers should include five copies of abstracts, as described above, of major current investigative work. A letter from the laboratory director, or appropriate administrative officer, approving the application is also necessary.

Society News.—At the annual meeting of the **National Gastroenterological Association** in Los Angeles Dr. Sigurd W. Johnsen, Passaic, N. J., assumed the presidency; Dr. Lynn A. Ferguson, Grand Rapids, Mich., was named president-elect; and Drs. James T. Nix, New Orleans, Arthur A. Kirchner, Los Angeles, C. Wilmer Wirts, Philadelphia, and Frank J. Borrelli, New York, were chosen as vice-presidents. Reelected were Dr. A. Xerxes Rossien, Kew Gardens, N. Y., secretary, Dr. Roy Upham, New York, secretary-general, and Dr. Elihu Katz, New York, treasurer. Dr. Samuel Weiss, New York, was renamed as editor-in-chief of *The Review of Gastroenterology*. The 19th annual convention of the association will be held in Washington, D. C., in October, 1954.——At the annual meeting in Chicago the **College of American Pathologists** elected the following new governors: Drs. Cyrus C. Erickson, Memphis; John J. Clemmer, Albany, N. Y.; Donald A. Nickerson, Salem, Mass.; James W. Kernohan, Rochester, Minn.; and Allen R. Moritz, Cleveland.——At the annual meeting in Nashville the **National Medical Association** installed Dr. A. Porter Davis, Kansas City, Kan., as president and named Dr. Matthew Walker, Nashville, president-elect; Drs. John G. Thornton, Little Rock, Ark., Evan A. Gilkes, Baltimore, and

George B. Lennox, Omaha, vice-presidents, and Dr. Eugene T. Taylor, St. Louis, treasurer.——At the annual business session in Chicago the **American Association of Blood Banks** elected the following officers: president, Dr. Aaron Kellner, New York; vice-president, Dr. John R. Upton, San Francisco; president-elect, Dr. Merlin L. Trumbull, Memphis, Tenn. Named as district directors were Dr. Peter Vogel, New York, Dr. Coye C. Mason, Chicago, Dr. John H. Carlquist, Salt Lake City, and Dr. William C. Levin, Galveston, Texas. Re-elected for treasurer and secretary respectively were Mrs. Bernice Hemphill, San Francisco, and Miss Marjorie Saunders, Dallas, Texas. The 1954 meeting is scheduled for Sept. 13-15 at the Shoreham Hotel, Washington, D. C.——The **North Pacific Surgical Association** held its 40th annual meeting Nov. 20-21 in Victoria, B. C., under the presidency of Dr. Thomas M. Jones of Victoria, B. C. Presentations included "Use of Radioactive Isotopes in Surgery," "Present Status of Vascular Grafts," "Further Studies on the Billroth I Operation for Peptic Ulcer," and "Importance of a Short Afferent Loop in Gastrectomy for Peptic Ulcer: a Study of the Protective Mechanisms Involved."——At the annual meeting in Kansas City, Mo., the **Mid-Continent Psychiatric Association** elected the following officers: president, Dr. Clarence J. Kurth, Wichita, Kan.; vice-president and president-elect, Dr. Paul S. Hines, Kansas City, Mo.; secretary-treasurer, Dr. Frank F. Merker, Topeka, Kan.; councilors, Drs. Robert G. Carnahan, Little Rock, Ark., William Rottersman, Topeka, Kan., G. Wilse Robinson Jr., Kansas City, Mo., and Harold G. Sleeper, Oklahoma City.——At the annual meeting in Minneapolis the **Mississippi Valley Trudeau Society** elected the following officers: president, Dr. Ralph I. Canuteson, Lawrence, Kan.; president-elect, Dr. Ejvind P. Fenger, Minneapolis; vice-president, Dr. Leon J. Galinsky, Des Moines, Iowa; and secretary-treasurer, Dr. Jesse A. Stocker, Springfield, Ill. William H. Feldman, D.V.M., Rochester, Minn., was awarded the Dearholt medal for outstanding work done in the development of streptomycin as a chemotherapeutic agent in the treatment of tuberculosis.——At the annual meeting in Chicago the **American Society for the Study of Arteriosclerosis** elected the following officers: president, Dr. Russell L. Holman, New Orleans; vice-president, Dr. Louis N. Katz, Chicago; and secretary-treasurer, Dr. O. J. Pollak, Dover, Del.——At a recent meeting of the **Baltimore-Washington Dermatological Society** the following officers were elected for a term of one year: chairman, Dr. Israel Zeligman, Baltimore; vice-chairman, Dr. Jack L. Derzavis, Washington, D. C.; and secretary-treasurer, Dr. Raymond C. V. Robinson, Baltimore.——The **New England Society of Anesthesiologists** met on Dec. 4 at the submarine base, New London, Conn., for the following program:

Decompression Sickness, Commander Gerald J. Duffner, Washington, D. C.
Explanatory Talk with Slides on Submarine Escape Training.
Demonstration of Submarine Escape Training Tank.
Underwater Respiratory Apparatus, Lieut. P. P. Newman.
Oxygen Poisoning, Commander Jack L. Kinsey.
Carbon Dioxide Toxicity and Oxygen Requirements, Karl E. Schaeffer.

LATIN AMERICA

Medical Meeting of French-Speaking Countries.—The third Medical Congress of French-Speaking Countries in the Caribbean will meet jointly with the Haitian Chapter of the International College of Surgeons, Dec. 15-21, at Port-au-Prince, Haiti. For information write Dr. Constant Pierre-Louis, School of Medicine, Port-au-Prince, Haiti.

FOREIGN

Prize for Medicosurgical Films.—The annual prize for medicosurgical cinema of 100,000 francs (about $290) and other awards will be given during the last session of the course on "Actualités médico-chirurgicales" at the Faculté de Médecine de Paris in March, 1954. The prizes are offered only for amateurs' films, unpublished, not subsidized, and not produced by any laboratory or firm. Films may be silent or sound, in black and white, or in color but must be 16 mm. Films must reach La Presse Médicale, 120, Boulevard Saint-Germain, Paris VIe, before March 8, 1954.

MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. George F. Lull, 535 North Dearborn St., Chicago 10, Secretary.

1954 Annual Meeting, San Francisco, June 21-25.

1954 Clinical Meeting, Miami, Florida, Nov. 30-Dec. 3.

1955 Annual Meeting, Atlantic City, N. J., June 6-10.

1955 Clinical Meeting, Boston, Nov. 29-Dec. 2.

AMERICAN ACADEMY OF DERMATOLOGY AND SYPHILOLOGY, Palmer House, Chicago, Dec. 5-10. Dr. John E. Rauschkolb, P. O. Box 6565, Cleveland 1, Secretary.

AMERICAN ACADEMY OF OBSTETRICS AND GYNECOLOGY, Netherland Plaza Hotel, Cincinnati, Dec. 14-16. Dr. C. Paul Hodgkinson, 116 South Michigan Blvd., Chicago 3, Secretary.

AMERICAN FEDERATION FOR CLINICAL RESEARCH:

EASTERN SECTION, Amphitheater, Children's Medical Center, Boston, Jan. 4. Dr. Walter Judson, Evans Memorial Hospital, Boston, Chairman.

SOUTHERN SECTION, Jung Hotel, New Orleans, Jan. 29. Dr. William Parson, University of Virginia School of Medicine, Charlottesville, Va., Chairman.

WESTERN SECTION, Auditorium, University of Oregon Medical School, Portland, Ore., Jan. 28. Dr. I. S. Edelman, University of California Medical Center, San Francisco Hospital, San Francisco 15, Secretary.

AMERICAN LARYNGOLOGICAL, RHINOLOGICAL AND OTOLOGICAL SOCIETY:

EASTERN SECTION, Waldorf-Astoria, New York, Jan. 8. Dr. Francis W. Davison, Danville, Pa., Chairman.

MIDDLE SECTION, Park Plaza Hotel, St. Louis, Jan. 18. Dr. Ralph J. McQuiston, 20 North Meridian St., Indianapolis 4, Chairman.

SOUTHERN SECTION, Brown Hotel, Louisville, Ky., Jan. 16. Dr. Lester A. Brown, 490 Peachtree St., N.E., Atlanta 3, Ga., Chairman.

AMERICAN SOCIETY FOR SURGERY OF THE HAND, Palmer House, Chicago, Jan. 22. Dr. George V. Webster, 960 East Green St., Pasadena 1, Calif., Secretary.

ASSOCIATION FOR RESEARCH IN NERVOUS AND MENTAL DISEASES, Hotel Roosevelt, New York, Dec. 11-12. Dr. Clarence C. Hare, 710 West 168th St., New York 32, Secretary.

NORTHWEST SOCIETY FOR CLINICAL RESEARCH, Portland, Ore., Jan. 28. Dr. Arthur L. Rogers, 1216 S.W. Yamhill St., Portland, Ore., Secretary.

RADIOLOGICAL SOCIETY OF NORTH AMERICA, Palmer House, Chicago, Dec. 13-18. Dr. Donald S. Childs, 713 East Genesee St., Syracuse 2, N. Y., Secretary.

REGIONAL MEETINGS, AMERICAN COLLEGE OF PHYSICIANS:

EASTERN PENNSYLVANIA, Philadelphia, Jan. 15. Dr. Thomas M. McMillan, 330 S. Ninth St., Philadelphia 7, Governor.

SOUTHERN SURGICAL ASSOCIATION, The Homestead, Hot Springs, Va., Dec. 8-10. Dr. John C. Burch, 2112 West End Ave., Nashville 5, Tenn., Secretary.

WESTERN SOCIETY FOR CLINICAL RESEARCH, Portland, Ore., Jan. 29-30. Dr. Herbert N. Hultgren, Stanford Hospital, San Francisco 15, Secretary.

FOREIGN

ASSOCIATION OF SURGEONS OF GREAT BRITAIN AND IRELAND, Leeds, England, May 13-15, 1954. Dr. Henry W. S. Wright, 45 Lincoln's Inn Fields, London W.C.2, England, Honorary Secretary.

BRITISH MEDICAL ASSOCIATION, Glasgow, Scotland, July 1-9, 1954. Dr. A. Macrae, B.M.A. House, Tavistock Square, London, W.C.1, England, Secretary.

CANADIAN MEDICAL ASSOCIATION, Vancouver, B. C., Canada, June 18-22, 1954. Dr. T. C. Routley, 135 St. Clair Ave. W., Toronto 5, Ont., Canada, General Secretary.

CONFERENCE OF INTERNATIONAL UNION AGAINST TUBERCULOSIS, Madrid, Spain, Sept. 26-Oct. 2, 1954. Secretariat, Escuela de Tisiologia, Ciudad Universitaria, Madrid, Spain.

CONGRESS OF INTERNATIONAL ASSOCIATION FOR THE PREVENTION OF BLINDNESS, New York, N. Y., U. S. A., Sept. 12-17, 1954. Professor Franceschetti, 2 Avenue Mirmot, Geneva, Switzerland, Secretary-General.

CONGRESS OF INTERNATIONAL SOCIETY OF SURGERY, Paris, France, May 21-22, 1954. Dr. L. Dejardin, 141, rue Belliard, Brussels, Belgium, General Secretary.

FRENCH MEDICAL CONGRESS OF FRENCH SPEAKING COUNTRIES IN THE CARIBBEAN, Port-au-Prince, Haiti, Dec. 15-21. For information write: Dr. Constant Pierre-Louis, School of Medicine, Port-au-Prince, Haiti.

HEALTH CONGRESS OF THE ROYAL SANITARY INSTITUTE, Scarborough, England, April 27-30. Mr. P. Arthur Wells, Royal Sanitary Institute, 90 Buckingham Palace Road, London, S.W.1, England, Secretary.

INTERNATIONAL CANCER CONGRESS, Sao Paulo, Brazil, July 23-29, 1954. Prof. A. Prudente, 171 rua Benjamin Constante, Sao Paulo, Brazil, President.

INTERNATIONAL CONFERENCE ON THROMBOSIS AND EMBOLISM, Basle, Switzerland, July 15-19, 1954. Dr. W. Merz, Chief Medical Officer, Gynecological Clinic, University of Basle, Basle, Switzerland, Hon. Secretary.

INTERNATIONAL CONGRESS ON CHILD PSYCHIATRY, University of Toronto, Toronto, Ontario, Canada, Aug. 13-14, 1954. Miss Helen Speyer, International Association for Child Psychiatry, 1790 Broadway, New York 19, New York, U. S. A., Executive Officer.

INTERNATIONAL CONGRESS OF CLINICAL PATHOLOGY, Washington, D. C., U. S. A., Sept. 6-10, 1954. Dr. Robert A Moore, Washington University School of Medicine, St. Louis 10, Missouri, U. S. A., Chairman, Committee on Arrangements.

INTERNATIONAL CONGRESS ON DISEASES OF THE CHEST, Barcelona, Spain, Oct. 4-8, 1954 Mr. Murray Kornfeld, 112 East Chestnut St., Chicago 11, Illinois, Executive Secretary.

INTERNATIONAL CONGRESS ON GROUP PSYCHOTHERAPY, Toronto, Ont., Canada, Aug. 12-14, 1954. Dr. J. L. Moreno, Room 327, 101 Park Ave., New York 17, N. Y., U. S. A., Director of Organizing Committee.

INTERNATIONAL CONGRESS OF HEMATOLOGY, Paris, Sept. 6-11, 1954. Dr. Jean Bernard, 86 rue d'Assas, Paris 6e, France, Secretary.

INTERNATIONAL CONGRESS OF THE HISTORY OF MEDICINE, Rome and Salerno, Italy, Sept. 13-20, 1954. For information write: Segreteria XIV Congresso Internazionale di Storia della Medicina, Instituto di Storia della Medicine, Citta Universitaria, Rome, Italy.

INTERNATIONAL CONGRESS OF HYDROCLIMATISM AND THALASSOTHERAPY, Dubrovnik, Yugoslavia, May 8-16, 1954. Prof. C. Plavsic, Zeleni venac 1, Belgrade, Yugoslavia, Secretary General.

INTERNATIONAL CONGRESS OF INDUSTRIAL MEDICINE, Naples, Italy, Sept. 13-19, 1954. Professor Scipione Caccuri, Director, Institute of Industrial Medicine Policlinico, Naples, Italy, Chairman, Organizing Committee.

INTERNATIONAL CONGRESS OF INTERNAL MEDICINE, Stockholm, Sweden, Sept. 15-18, 1954. Professor Anders Kristenson, Karolinska Sjukhuset, Stockholm 60, Sweden, Secretary-General.

INTERNATIONAL CONGRESS OF INTERNATIONAL COLLEGE OF SURGEONS, Sao Paulo, Brazil, April 26-May 2, 1954. Dr. Max Thorek, 1516 Lake Shore Drive, Chicago, Illinois, U. S. A., Secretary-General.

INTERNATIONAL CONGRESS ON MENTAL HEALTH, University of Toronto, Toronto, Ontario, Canada, Aug. 14-21, 1954. For information write: Executive Officer, International Congress on Mental Health, 111 St. George St., Toronto, Ontario, Canada.

INTERNATIONAL CONGRESS OF NUTRITION, Amsterdam, Netherlands, Sept. 14-18, 1954. For information write: Dr. M. van Eekelen, Centraal Instituut voor Voedingsonderzoek T.N.O., 61 Catharynesingel, Utrecht, Netherlands.

INTERNATIONAL CONGRESS ON OBSTETRICS AND GYNECOLOGY, Geneva, Switzerland, July 26-31, 1954. Dr H. de Watteville, Maternité Hôpital Cantonal, Geneva, Switzerland, President.

INTERNATIONAL CONGRESS OF OPHTHALMOLOGY, University of Montreal and McGill University, Montreal, Canada, Sept. 10-11, 1954, and Waldorf-Astoria, New York, N. Y., U. S. A., Sept. 12-17, 1954. Dr. William L. Benedict, 100 First Avenue Building, Rochester, Minnesota, U. S. A., Secretary-General.

INTERNATIONAL CONGRESS OF ORTHOPEDIC SURGERY AND TRAUMATOLOGY, Berne, Switzerland, Aug. 30-Sept. 3, 1954. For information write: Professor M. Dubois, Isle-Hospital, Berne, Switzerland.

INTERNATIONAL CONGRESS OF PSYCHOLOGY, Montreal, Canada, June 7-12, 1954. For information write: Prof. H. S. Langfeld, International Union of Scientific Psychology, Eno Hall, Princeton University, Princeton, N. J., U. S. A.

INTERNATIONAL CONGRESS FOR PSYCHOTHERAPY, Zurich, Switzerland, July 21-24, 1954. Dr. H. K. Fierz, Theaterstrasse 12, Zurich 1, Switzerland, Secretary General.

INTERNATIONAL GERONTOLOGICAL CONGRESS, London and Oxford, England, July 12-22, 1954. Prof. R. E. Tunbridge, General Infirmary, Department of Medicine, The University, Leeds, England, President.

INTERNATIONAL POLIOMYELITIS CONGRESS, Rome, Italy, Sept. 6-10, 1954. Mr. Stanley E. Henwood, 120 Broadway, New York 5, N. Y., U. S. A., Executive Secretary.

INTERNATIONAL SOCIETY OF BLOOD TRANSFUSION, Paris, France, Sept. 12-19, 1954. For information write: Colonel Julliard, Societe Internationale de Transfusion Sanguine, 53 Boulevard Diderot, Paris 12e, France.

INTERNATIONAL SOCIETY FOR CELL BIOLOGY, Leiden, Netherlands, Sept. 2-9, 1954. Professor Peter J. Gaillard, University of Leiden, Leiden, Netherlands, Secretary.

INTERNATIONAL SOCIETY OF GEOGRAPHICAL PATHOLOGY, Washington, D. C., U. S. A., Sept. 6-10, 1954. Professor Fred C. Roulet, Hebelstrasse 24, Basle, Switzerland, Secretary-General.

JOURNEES MEDICALES, Paris, France, April 21-25, 1954. For information write: Secretariat of the Journees, 12, rue Pierre-Geofroix, Colombes (Seine) France.

LATIN AMERICAN CONGRESS OF OTORHINOLARYNGOLOGY, Caracas, Venezuela, Feb. 21-25, 1954. Dr. Victorino Marquez Reveron, Centro, Medico, Caracas, Venezuela, Secretary-General.

LATIN AMERICAN CONGRESS OF PHYSICAL MEDICINE, Medellin, Columbia, South America, Feb. 15-20, 1954. Dr. Cassius Lopez de Victoria, 176 East 71st St., New York 21, N. Y., U. S. A., Executive Director.

PAN AMERICAN CONGRESS OF OTORHINOLARYNGOLOGY AND BRONCHOESOPHAGOLOGY, Mexico, D.F., Mexico, Feb. 28-March 4, 1954. Dr. Pedro Hernandez Gonzalo, 8 No. 358, Vedado, Havana, Cuba, General Secretary.

PAN AMERICAN MEDICAL ASSOCIATION, International Medical Cruise Congress, S. S. Nieuw Amsterdam, Jan. 6-22, 1954. Dr. Joseph J. Eller, 745 Fifth Avenue, New York 22, N. Y., U. S. A., Executive Director.

PAN-PACIFIC SURGICAL CONGRESS, Honolulu, Hawaii, Oct. 7-18, 1954. Dr. F. J. Pinkerton, Suite 7, Young Bldg., Honolulu 13, Hawaii, Director General.

PERSIAN GULF MEDICAL SOCIETY, Dhahran, Saudi Arabia, Dec. 7-8. Dr. N. J. Conan Jr., Department of Internal Medicine, Arabian American Oil Company, Dhahran, Saudi Arabia, Secretary.

SECTIONAL MEETING, AMERICAN COLLEGE OF SURGEONS, London, England, May 17-19, 1954. Dr. Michael L. Mason, 40 East Erie St., Chicago 11, Ill., U. S. A., Secretary.

SOUTH AMERICAN CONGRESS OF ANGIOLOGY, Sao Paulo, Brazil, July 1954. For information write: Dr. Rubens Carlos Mayall, Rua Senador Vergueiro 73, Rio de Janeiro, Brazil, S. A.

WORLD CONGRESS OF CARDIOLOGY, Washington, D. C., and Bethesda, Md., U. S. A., Sept. 12-17, 1954. Dr. L. W. Gorham, 44 East 23d St., New York 10, N. Y., U. S. A., Secretary-General.

WORLD CONGRESS OF INTERNATIONAL SOCIETY FOR THE WELFARE OF CRIPPLES, The Hague, Netherlands, Sept. 13-17, 1954. For information write: D. C. Schaap, Centrale Vereniging, Apeldoorschweg 51, Arnhem, Netherlands.

WORLD FEDERATION OF OCCUPATIONAL THERAPISTS, Edinburgh, Scotland, August 17, 1954.

WORLD MEDICAL ASSOCIATION, Rome, Italy, Sept. 26-Oct. 2, 1954. Dr. Louis H. Bauer, 345 East 46th St., New York 17, N. Y., U. S. A., Secretary-General.

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EXAMINATIONS AND LICENSURE

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: *Written.* Various Centers, July 16. Sec., Dr. Curtiss B. Hickox, 80 Seymour St., Hartford 15.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: *Oral.* Chicago, May or June. Final date for filing application is Jan. 15. Sec., Dr. Leonard T. Furlow, 600 S. Kingshighway, St. Louis 10.

AMERICAN BOARD OF NEUROLOGY AND PSYCHIATRY: *Psychiatry and Neurology.* Dec. 14-15. Applications no longer being accepted. Chicago, April 29-30. Final date for filing application is Feb. 1. Sec., Dr. David A. Boyd, Jr., 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: Written examination and review of case histories for all candidates will be held in various cities of the United States, Canada, and military centers outside the continental United States on Feb. 5. Case abstracts are to be sent by the candidate to the Secretary as soon as possible after receiving notification of eligibility to the Part I written examination. *Oral.* Chicago, Oct. 1. Application for reexamination in Part II must be made prior to Feb. 1 of any year. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

AMERICAN BOARD OF OPHTHALMOLOGY: *Written.* Various Centers, January 25-26, 1954. Final date for filing applications was July 1. *Practical.* San Francisco, June 25-29; New Orleans, Feb. 5-11, 1955. Final date for filing application for 1955 written examination is July 1. Sec., Dr. Edwin B. Dunphy, 56 Ivie Road, Cape Cottage, Maine.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: *Part II.* Chicago, Jan. 20-22. Final date for filing application was August 15. Final date for filing application for Part I is Nov. 30. Sec., Dr. Harold A. Sofield, 122 S. Michigan Ave., Chicago 3.

AMERICAN BOARD OF OBSTETRICS: *Written.* Selected Places, Jan. 15. This is the only written examination which will be given during 1954. *Oral.* Washington, D. C., Feb. 19-21; Des Moines, March 19-21; New York City, May 1-3; San Francisco, June 25-27; Chicago, Oct. 8-10 and New Haven, December.

AMERICAN BOARD OF RADIOLOGY: *Oral. Radiology, Roentgenology, Diagnostic Roentgenology and Therapeutic Radiology.* Chicago, Dec. 6-11. Final date for filing application was July 1. Sec., Dr. B. R. Kirklin, 102-110 Second Ave. S.W., Rochester, Minn.

AMERICAN BOARD OF UROLOGY: *Oral-clinical and pathology.* Chicago, Feb. 17-20. Sec., Dr. Harry Culver, 30 Westwood Road, Minneapolis 16.

DEATHS

Davison, Thomas Callahan ⊕ Atlanta, Ga.; born in Woodville, Ga., Nov. 13, 1883; Atlanta College of Physicians and Surgeons, 1906; an Associate Fellow of the American Medical Association; an honorary member of the International College of Surgeons; member of the Southern Surgical Association, Southeastern Surgical Congress of which he was past president, and the American Association for Thoracic Surgery; past president of the American Goiter Association and Medical Alumni of Emory University; fellow of the American College of Surgeons; member of the founders group of the American Board of Surgery; specialist certified by the American Board of Thoracic Surgery; formerly associate professor of clinical surgery at Emory University School of Medicine; served during World War I; for many years chief of surgical service at Grady Hospital; affiliated with Georgia Baptist Hospital; died Sept. 17, aged 69, of congestive heart failure.

Danzis, Maximillian ⊕ Newark, N. J.; born in 1874; University and Bellevue Hospital Medical College, New York, 1899; a trustee and past president of the Academy of Medicine of Northern New Jersey; past president of the Essex County Medical Society and the New Jersey Society of Surgeons; specialist certified by the American Board of Surgery; fellow of the American College of Surgeons; co-founder and visiting surgeon, Newark Beth Israel Hospital; consulting surgeon, Presbyterian Hospital in Newark, Essex County Hospital for Contagious Diseases in Belleville, Essex County Sanatorium in Verona, and the Irvington General Hospital; served as a trustee of the old Newark University and of the American Hebrew University of New York; in 1941 received the Edward J. Ill award for "extraordinary service as a physician and citizen"; died Oct. 20, aged 79, of acute coronary thrombosis.

Reed, Horace ⊕ Oklahoma City; born Sept. 26, 1876; University of Missouri School of Medicine, Columbia, 1901; member of the House of Delegates of the American Medical Association from 1929 to 1937; past president of the Oklahoma City Academy of Medicine and the Oklahoma County Medical Society; fellow of the American College of Surgeons; member of the founders group of the American Board of Surgery; at one time professor of clinical surgery at the University of Oklahoma School of Medicine; captain in the U. S. Army during World War I, and chairman of the medical examiners board for Oklahoma County during World War II; affiliated with St. Anthony and University hospitals; died Oct. 7, aged 77, of uremia and hypertrophy of the prostate.

Londrigan, Joseph Francis ⊕ Hoboken, N. J.; born in Hoboken, N. J., in 1884; University of Pennsylvania School of Medicine, Philadelphia, 1910; member of the House of Delegates of the American Medical Association from 1948 to 1953; fellow of the American College of Surgeons; past president and vice-president of the Medical Society of New Jersey; consulting surgeon, Holy Name Hospital, Teaneck, Bayonne (N. J.) Hospital, North Hudson Hospital, Union City, and Jersey City Medical Center; for many years affiliated with St. Mary's Hospital, where he died Oct. 17, aged 69, of cirrhosis of the liver, arteriosclerotic heart disease, and benign prostatic hypertrophy.

Chamberlin, Donald Tillinghast ⊕ Knoxville, Tenn.; Washington University School of Medicine, St. Louis, 1930; certified by the National Board of Medical Examiners; specialist certified by the American Board of Internal Medicine; member of the American Gastro-Enterological Association; fellow of the American College of Physicians; served during World War II; formerly practiced in Boston, where he was on the staff of the New England Deaconess Hospital, Boston City Hospital, and the New England Baptist Hospital, where he died Oct. 1, aged 48, of portal cirrhosis, thrombosis of the portal vein, and esophageal varices with rupture.

⊕ Indicates Member of the American Medical Association.

Catlett, Marshall Burr ⊕ Fort Wayne, Ind.; born in North Manchester, May 11, 1888; Indiana University School of Medicine, Indianapolis, 1913; past president of the Fort Wayne Medical Society; until recently vice-president, in 1952 president, and for 16 years a member of the city board of health; formerly councilor of the Twelfth District of the Indiana State Medical Association; during World War I medical officer of the Sixth Cameron Highlanders, an infantry division, and attained the rank of captain; at one time county health officer; member of the city planning commission; died in the Methodist Hospital Oct. 7, aged 65.

Canavan, Myrtelle Moore ⊕ Boston; born in St. Johns, Mich., in 1879; Woman's Medical College of Pennsylvania, Philadelphia, 1905; specialist certified by the American Board of Pathology; member of the New England Society of Psychiatry, International Association of Medical Museums, and the College of American Pathologists; fellow of the American College of Physicians; secretary-treasurer of the Massachusetts Medico-Legal Society; formerly curator of the Warren Anatomical Museum, Harvard Medical School, and assistant pathologist at Boston State Hospital; died Aug. 26, aged 74, of paralysis agitans.

Aguglia, Vincent B., Boston; Middlesex College of Medicine and Surgery, Cambridge, Mass., 1923; died in Watertown, Mass., Oct. 8, aged 55.

Alexander, George, Pontiac, Mich.; Detroit College of Medicine, 1894; died Oct. 2, aged 90, of cerebral hemorrhage.

Anderson, Axel Hjalmar, Detroit; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1907; also a graduate in pharmacy; died Oct. 18, aged 71, of cancer of the larynx and Paget's disease.

Blair, Harold Albert ⊕ Curwensville, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1906; on the courtesy staff of Clearfield Memorial Hospital, where he died Aug. 22, aged 74, of coronary heart disease.

Bowmer, Otho Cassius ⊕ Corsicana, Texas; Barnes Medical College, St. Louis, 1900; served as health officer of Navarro County; an officer in the U. S. Army during the Spanish-American War and World War I; for many years on the board of the Physicians and Surgeons Hospital; died Sept. 28, aged 79, of coronary thrombosis.

Bremer, Benjamin Franklin ⊕ Glenmora, La.; Medical Department of Tulane University of Louisiana, New Orleans, 1903; for many years town health officer; served on the staff of the Baptist Hospital in Alexandria; died Sept. 26, aged 75, of coronary occlusion.

Brock, Henry Herbert ⊕ Alfred, Maine; Medical School of Maine, Portland, 1890; fellow of the American College of Surgeons; formerly on the faculty of his alma mater; until recently consulting surgeon to the Maine General Hospital, Portland, Webber Hospital, Biddeford, and Goodall Hospital, Sanford; died Oct. 4, aged 89, of arteriosclerosis.

Brooks, Edward Benjamin, Oklahoma City, Okla.; Louisville National Medical College, Medical Department State University, 1908; assistant city physician; died in the Mercy Hospital Sept. 26, aged 66, of hypertensive heart disease.

Burgess, Marshall E. ⊕ Miami, Ariz.; Gate City Medical College, Texarkana, Ark., 1903; past president of the Gila County Medical Society; mayor of Miami; on the staff of the Gila General Hospital; formerly associated with the Indian Service; died in Phoenix, Ariz., Sept. 23, aged 74.

Burgner, Benjamin H. ⊕ Chicago; Chicago College of Medicine and Surgery, 1916; on the staff of the Garfield Park Community Hospital, where he died Oct. 15, aged 75, of pulmonary tuberculosis.

Campbell, Hiram Gill ✠ Tecumseh, Okla.; University of Nashville (Tenn.) Medical Department, 1903; past president and secretary of the Pottawatomie County Medical Society; died in Lebanon, Tenn., Oct. 2, aged 81, of a heart attack.

Christophe, Herman C. ✠ Manchester, N. H.; Boston University School of Medicine, 1900; affiliated with Elliot and Notre Dame de Lourdes hospitals; died Oct. 1, aged 79, of arteriosclerotic heart disease.

Clark, Richard Harry ✠ Hattiesburg, Miss.; Tulane University of Louisiana School of Medicine, New Orleans, 1924; vice-president of the Mississippi State Medical Association; fellow of the American College of Surgeons; on the staffs of the Methodist Hospital and the South Mississippi Infirmary; died Sept. 23, aged 54.

Coe, Marie Condee, Los Angeles; University of Southern California School of Medicine, Los Angeles, 1952; certified by the National Board of Medical Examiners; pediatric resident at Los Angeles County General Hospital; killed in an automobile accident Aug. 5, aged 27.

Conklin, Rush West ✠ Washington, D. C.; George Washington University School of Medicine, Washington, 1909; died Nov. 2, aged 76.

Cornet, Louis Anthony ✠ Washington, D. C.; Georgetown University School of Medicine, Washington, 1921; member of the American Academy of General Practice; died Oct. 28, aged 56.

Davies, Matthew Wray ✠ Delaware, Ohio; Starling-Ohio Medical College, Columbus, 1910; member of the American Academy of General Practice; served as county coroner; affiliated with Jane M. Case Hospital, where he died Oct. 17, aged 67, of cerebrovascular hemorrhage.

Dickinson, Charles Baldwin, Little Rock, Ark.; Eclectic Medical University, Kansas City, Mo., 1918; Kansas City (Mo.) College of Medicine and Surgery, 1923; served during World War I and was awarded the Purple Heart; died in Hot Springs National Park Oct. 13, aged 60, of cerebral hemorrhage.

Doles, James Wesley ✠ Knoxville, Iowa; Northwestern University Medical School, Chicago, 1936; member of the American Psychiatric Association; past president of the Marion County Medical Society; served during World War II; affiliated with the Veterans Administration Hospital; died in the Veterans Administration Hospital in Des Moines Sept. 21, aged 44, of carcinoma of the liver and lung.

Eigler, Charles O. ✠ Englewood, Colo.; Drake University Medical Department, Des Moines, Iowa, 1888; died in Englewood Aug. 11, aged 85, of acute coronary occlusion.

Flynn, David Storrs, Monmouth Beach, N. J.; Columbia University College of Physicians and Surgeons, New York, 1904; died in Dr. E. C. Hazard Hospital, Long Branch, Aug. 19, aged 73, of arteriosclerotic heart disease.

Francis, John Wesley ✠ Perry, Okla.; University of Oklahoma School of Medicine, Oklahoma City, 1911; past president of the Kay-Noble Counties Medical Society; served as health officer of Noble County; on the staff of Perry Memorial Hospital; died Oct. 8, aged 72, of coronary infarction.

Gammill, James L., Haslet, Texas; Fort Worth School of Medicine, Medical Department of Texas Christian University, 1900; died in Denton Sept. 12, aged 83, of congestive heart failure.

Goggins, Robert Joseph ✠ Oconto Falls, Wis.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1899; served during World War I; died Sept. 23, aged 77, of cerebral hemorrhage.

Haight, Julius Eugene, Walpole, Mass.; Albany (N. Y.) Medical College, 1899; served during World War I; school physician; for many years chief of staff, Highland Hospital in Beacon, N. Y.; died Oct. 7, aged 76, of coronary occlusion.

Harlan, Lee Henry, Chicago; Illinois Medical College, Chicago, 1910; died Oct. 20, aged 73, as the result of a fall from a third floor window.

Kapner, Zadok, New York City; New York Homeopathic Medical College and Flower Hospital in New York, 1917; affiliated with Park East and Beth David hospitals; died Oct. 20, aged 71.

King, Hubert Charles ✠ Lakewood, Ohio; Western Reserve University School of Medicine, Cleveland, 1914; fellow of the American College of Physicians; past president of the Academy of Medicine of Cleveland; director of medicine, emeritus, Fairview Park Hospital; died in Lakewood Hospital Oct. 17, aged 64, of pneumonia.

Lavy, William S., Gridley, Calif.; Hahnemann Medical College of the Pacific, San Francisco, 1904; city health officer; died Oct. 9, aged 81, of coronary occlusion.

Layton, Roy Wilfred, Melrose, Mass.; University of Kansas School of Medicine, Kansas City, Kan., 1913; fellow of the American College of Surgeons; on the staff of the Melrose Hospital; died Sept. 25, aged 65, of myocardial infarction.

Legat, Mary B. ✠ Fox River Grove, Ill.; Illinois Medical College, Chicago, 1908; affiliated with Women and Children's Hospital, Chicago, where she died Oct. 28, aged 82, of hypostatic pneumonia, arteriosclerotic heart disease, and diabetes.

Levin, Harry Maurice ✠ Waterloo, Iowa; John A. Creighton Medical College, Omaha, 1919; affiliated with St. Francis Hospital; died Aug. 13, aged 57, of coronary disease.

Lewis, John Francis ✠ La Salle, Ill.; University Medical College of Kansas City, Mo., 1905; an Associate Fellow of the American Medical Association; past president of the North Central Illinois Medical Association; affiliated with St. Mary's Hospital in La Salle and St. Margaret's Hospital in Spring Valley; died Oct. 9, aged 74, of coronary occlusion.

Matthews, Duncan Newton ✠ Columbia, S. C.; Medical College of the State of South Carolina, Charleston, 1909; for many years physician for the University of South Carolina boxing team; died in the Baptist Hospital Oct. 15, aged 77.

Moore, George Henry ✠ Upper Darby, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1893; member of the American Academy of Ophthalmology and Otolaryngology; died Oct. 1, aged 81.

Myller, Ernest ✠ New York; Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin, Germany, 1919; specialist certified by the American Board of Obstetrics and Gynecology; affiliated with Madison Avenue and University hospitals; died Oct. 23, aged 60, of acute coronary occlusion.

O'Dwyer, Joseph, Staten Island, N. Y.; Columbia University College of Physicians and Surgeons, New York, 1900; served during World War I; an examiner for draft boards during World War II; at one time on the staff of New York Foundling Hospital; died Oct. 19, aged 78.

Pence, Charles W., Philadelphia; University of Maryland School of Medicine, Baltimore, 1894; medical examiner for the Baltimore and Ohio Railroad; died in the Shenandoah County Memorial Hospital, Woodstock, Va., Oct. 7, aged 83, of coronary thrombosis.

Placa, James Anthony ✠ Ridgewood, N. J.; Temple University School of Medicine, Philadelphia, 1936; died in Atlantic City Hospital Oct. 25, aged 45, of acute coronary occlusion.

Price, Stanley Francis, Chicago; Loyola University School of Medicine, Chicago, 1918; died in Bay Pines Hospital, St. Petersburg, Fla., Nov. 1, aged 59.

Ramey, Cash Clay Jr. ✠ Portales, N. M.; Rush Medical College, Chicago, 1942; served during World War II; participated in five major campaigns in the European Theater, and received several decorations including the Purple Heart for serious wounds received in action; member of the Roosevelt General Hospital; died Oct. 10, aged 36, of a heart attack.

Reeve, James Spofford ✠ Appleton, Wis.; College of Physicians and Surgeons, medical department of Columbia College, New York, 1889; died July 22, aged 88, of cardiovascular renal disease and arteriosclerosis.

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Robertson, Jackson Comer, Modesto, Calif.; Vanderbilt University School of Medicine, Nashville, Tenn., 1898; fellow of the American College of Surgeons; served during World War I; died Oct. 7, aged 81, of cerebral hemorrhage.

Rose, Bert Andrew, Dayton, Ohio; Howard University College of Medicine, Washington, D. C., 1912; formerly member of the state board of medical examiners; affiliated with Miami Valley and St. Elizabeth hospitals; awarded an honorary master of science degree by Wilberforce University, Wilberforce, Ohio; died Oct. 21, aged 68, of carcinoma of the right kidney.

Schuricht, Gustav M., St. Louis; Washington University School of Medicine, St. Louis, 1896; died in Lutheran Hospital Oct. 15, aged 79, of acute gangrenous appendicitis, peritonitis, and coronary artery disease.

Scott, James Jacob, Durand, Wis.; American College of Medicine and Surgery, Chicago, 1906; died Oct. 12, aged 74, of aortic and mitral regurgitation and ventricular dilatation.

Twohig, John Elmer ✠ Fond du Lac, Wis.; Marquette University School of Medicine, Milwaukee, 1913; member of the American Academy of General Practice; on the staff of St. Agnes Hospital; died Aug. 14, aged 66, of adenocarcinoma of the cecum.

Uhr, Jacques Stanley ✠ New Brunswick, N. J.; Fordham University School of Medicine, New York, 1914; fellow of the American Academy of Pediatrics; served during World War I; for many years affiliated with St. Peter's Hospital, where he was director of pediatrics; at one time assistant in diseases of children, Columbia University College of Physicians and Surgeons in New York; died Oct. 9, aged 61, of carcinoma of the stomach.

Uzmann, Francis Joseph Jr. ✠ Lieutenant Commander, U. S. Navy, Queens Village, N. Y.; Hahnemann Medical College and Hospital of Philadelphia, 1943; honorably discharged from the U. S. Navy April 11, 1952, after serving with the Marines; served during World War II and also in Korea; died in Westhampton Beach, N. Y., Sept. 9, aged 39, of cirrhosis of the liver.

Valens, John Douglas ✠ Modesto, Calif.; University of Manitoba Faculty of Medicine, Winnipeg, Canada, 1941; specialist certified by the American Board of Orthopaedic Surgery; affiliated with Modesto City Hospital and Stanislaus County Hospital; died in Sun Valley, Idaho, Oct. 7, aged 38, of injuries received in an automobile accident.

Waters, Donald ✠ Wisconsin Rapids, Wis.; Detroit College of Medicine, 1900; died in the Riverview Hospital Sept. 15, aged 82, of heart failure.

Watkins, Daniel Alvey, Hagerstown, Md.; University of Maryland School of Medicine, Baltimore, 1903; at one time county health officer and police commissioner of Hagerstown; past president of the Washington County Medical Society; affiliated with Washington County Hospital, where he was past president of the staff and where he died Sept. 29, aged 76, of cerebral thrombosis and paralysis agitans.

Webster, Albert Martin ✠ Portland, Ore.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1904; past president of the Oregon State Medical Society; formerly city physician; an honorary staff member of Emanuel Hospital, after serving as an active staff member for many years; died Oct. 8, aged 85, of cerebral thrombosis.

Webster, Margaret E. Burgess, Philadelphia; Hering Medical College, Chicago, 1896; affiliated with Germantown Hospital and the Hospital of the Woman's Medical College of Pennsylvania; died Oct. 18, aged 78, of bundle branch block and arteriosclerosis.

Wellbery, Edward Montgomery ✠ Richfield Springs, N. Y.; Cornell University Medical College, New York, 1907; died Oct. 10, aged 67, of acute coronary heart disease.

Whelan, Edmond Vincent, Springfield, Mass.; Tufts College Medical School, Boston, 1909; served during World War I; for many years school physician; affiliated with Mercy Hospital; died Sept. 13, aged 67, of coronary thrombosis and arteriosclerosis.

Whipple, Farrington Hasham ✠ Portland, Maine; Harvard Medical School, Boston, 1892; member of the Massachusetts Medical Society; died in the Mercy Hospital Oct. 3, aged 87, of arteriosclerotic heart disease and bronchopneumonia.

Wick, William Winfield ✠ Enumclaw, Wash.; the Hahnemann Medical College and Hospital, Chicago, 1904; served as health officer; died Sept. 14, aged 73, of a heart attack.

Wiedenman, Charles Edward H. ✠ Schenectady, N. Y.; Albany (N. Y.) Medical College, 1921; fellow of the American College of Surgeons; past president of the Schenectady County Medical Society; affiliated with St. Claire's Hospital and Ellis Hospital, where he died Sept. 25, aged 57, of arteriosclerotic heart disease and diabetes mellitus.

Wilcox, John Miller III ✠ Pitman, N. J.; Western Reserve University School of Medicine, Cleveland, 1930; member of the Endocrine Medical Association; died in Charity Hospital, Cleveland, Aug. 14, aged 46, of esophageal varices and cirrhosis of the liver.

Wilde, Salmon Perry ✠ New Bedford, Mass.; Boston University School of Medicine, 1910; served during World War I; past president of the consulting staff of Sassaquin Sanatorium; affiliated with Union Hospital in Fall River, Acushnet (Mass.) Hospital, and St. Luke's Hospital, where he died Aug. 18, aged 66, of coronary occlusion.

Wiley, Bert Earle, Beverly Hills, Calif.; McGill University Faculty of Medicine, Montreal, Canada, 1901; fellow of the American College of Surgeons; died Aug. 5, aged 77, of heart disease.

Willard, Edgar Harold, Great Cacapon, W. Va.; University of Maryland School of Medicine, Baltimore, 1908; served as health officer of Morgan County; died recently in Berkeley Springs, aged 66, of malignancy of the spine.

Williams, James Marcus, Warsaw, N. C.; University of Maryland School of Medicine, Baltimore, 1902; died July 30, aged 78, of coronary embolism.

DIED WHILE IN MILITARY SERVICE

Cocks, Charles Edward Jr. ✠ Colonel, (MC), U. S. Army, San Francisco; born in San Francisco May 31, 1908; University of California Medical School, San Francisco, 1933; interned at the Highland Hospital of Alameda County and Peralta Hospital in Oakland; served as associate clinical professor of medico-military sciences and tactics at his alma mater; entered the medical reserve corps of the U. S. Army as a first lieutenant on May 13, 1933; served during World War II; became a lieutenant colonel on Dec. 2, 1943; entered the medical corps of the regular army as a major July 15, 1946; formerly chief of public health and welfare for the Armed Forces Far East Command; in June, 1951, received the master's degree and in 1952 the degree of doctor of public health, both in hospital administration, from the University of California School of Public Health; died in the Letterman Army Hospital Sept. 29, aged 45, of coronary occlusion and myocardial infarction.

Graveline, Ernest Louis Jr., Pawtucket, R. I.; born in Pawtucket, April 15, 1922; University of Nebraska College of Medicine, Omaha, 1949; interned at the White Plains (N. Y.) Hospital; certified by the National Board of Medical Examiners; entered the U. S. Army March 16, 1943, and was discharged Feb. 10, 1946; in May, 1949, was commissioned a first lieutenant in the Medical Corps, U. S. Army Reserve; in June, 1950, was promoted to captain; attached to the Third Battalion, 23rd Infantry Regiment, Second Division; captured by the communists in Korea on May 18, 1951; died as a prisoner of war in a communist prison camp Oct. 15, 1951, aged 29.

GOVERNMENT SERVICES

ATOMIC ENERGY COMMISSION

Fellowships in Industrial Medicine.—Eight fellowships in industrial medicine will be offered by the U. S. Atomic Energy Commission for the 1954-1955 academic year. The fellowship program, which was begun by the AEC four years ago, is designed to provide advanced training and on-the-job experience for physicians in the field of industrial medicine, particularly in relation to the atomic energy industry. The fellowships are open to U. S. citizens who hold M.D. degrees from approved medical schools and who have had at least one year of internship. In exceptional cases, equivalent experience may be accepted in lieu of the internship requirement. Successful candidates must be investigated by the FBI and approved by the AEC before receiving fellowships. Awards are for one year's academic training at institutions offering approved graduate courses in industrial medicine that provide special training facilities in the health problems associated with the atomic energy program. Normally, fellows will be eligible for a second, or in-plant, training year on successful completion of the academic year. In-plant training will be given in medical departments of major AEC plants and laboratories. There is a critical need for qualified industrial physicians in atomic energy installations, and at the end of the two year training period fellows may find employment in the program. There will be no commitment, however, on the part of the AEC to continue the applicant's training beyond the first year or to provide employment for him on the completion of training. Fellows will not be obligated to take the second year of training or to seek employment with the AEC or its contractors. The stipend during the first year is $3,600, with $350 additional for a wife and for each dependent child. Tuition and laboratory fees will be paid. The stipend for the second year is $6,000, with no additional amounts for a wife or children. The program is administered for the AEC by the Atomic Energy Project of the School of Medicine and Dentistry, University of Rochester, Rochester, N. Y. Fellows are selected by a committee headed by Dr. Robert A. Kehoe, director, Institute of Industrial Health, University of Cincinnati, and medical director, Ethyl Corporation. Applications for 1954-1955 fellowships should be submitted by Jan. 1, 1954, to AEC Fellowships in Industrial Medicine, Atomic Energy Project, University of Rochester, School of Medicine and Dentistry, Rochester, N. Y.

ARMY

Award of Legion of Merit.—Col. Henry C. Harrell, chief of the diagnostic section of the x-ray service at Brooke Army Hospital, has been awarded the Legion of Merit for distinguished work as radiological consultant to the Army Surgeon of the Far East command. He was cited for outstanding service as chief of the radiology service at Tokyo Army Hospital, for professional competence and devotion to duty in serving the sick and wounded, and for skill in interpretation of x-ray examinations. In addition to other duties, Colonel Harrell planned and directed a radiological survey of prisoners of war on Koje-do and prepared a valuable study on incidence of disease in the group. He is a member of the American College of Radiology and of the Radiological Society of North America.

Hospital News.—Dr. Jacob Finesinger, professor of psychiatry, University of Maryland School of Medicine, addressed officer-students of the military neuropsychiatry class at the Medical Field Service School, Ft. Sam Houston, Texas, recently during a two day visit to Brooke Army Medical Center. Dr. Finesinger lectured on goal-directed psychotherapy. He also conducted a program on the doctor-patient relationship at the Brooke Army Hospital monthly professional staff meeting.

VETERANS ADMINISTRATION

Residencies Available at Indianapolis.—Several residencies are available in internal medicine, pathology, and psychiatry at the Veterans Administration Hospital, Indianapolis. The hospital, located on the campus of Indiana University Medical Center, is affiliated with the medical center, and has programs integrated with it. These residencies are fully approved by the specialty boards. The stipends are as follows: junior resident (first year) $2,640 per annum, intermediate resident (second year) $2,970 per annum, and senior resident (third and fourth years) $3,300 per annum. In addition, Korean veterans may be eligible for assistance under the G.I. training benefits. Applications for residency training or information in this regard may be obtained from Dr. Matthew Winters, Chairman, Dean's Committee, Indiana University Medical Center, 1040 W. Michigan St., Indianapolis, Ind., or D. R. Robinson, M.D., Chief, Professional Services, VA Hospital, 1481 W. 10th St., Indianapolis, Ind.

Personal.—Dr. Joseph I. Fitzsimmons, chief of professional services at the VA Hospital in Omaha, Neb., has been named manager of the 250-bed VA Hospital at Iron Mountain, Mich. He succeeds Dr. Carleton Bates, who retired Oct. 24, 1953.

MISCELLANEOUS

Members of the Hoover Medical Task Force.—The announcement of 12 more appointments completes the membership of the Hoover Commission task force on medical services. Earlier the commission named Mr. Chauncey McCormick, Chicago businessman, as chairman, and Dr. Edwin L. Crosby, also of Chicago, as research director. The third appointment announced earlier was that of Dr. Walter Martin, President-Elect of the American Medical Association. The following have accepted appointment to the remaining posts:

Dr. Francis J Braceland, formerly dean, Loyola University School of Medicine, Chicago, now psychiatrist at Institute of Living, Hartford, Conn.

Dr. Edward Delos Churchill, chief of general surgical service, Massachusetts General Hospital, Boston.

Dr. Michael DeBakey, chairman of department of surgery, Baylor University College of Medicine, Houston, Texas.

Dr. Evarts A. Graham, surgeon-in-chief, Barnes Hospital and Children's Hospital, St. Louis.

Dr. Alan Gregg, vice-president of Rockefeller Foundation, New York.

Dr. Paul R. Hawley, U. S. Army, retired, Chicago, director, American College of Surgeons, former chief medical director, Veterans Administration.

Dr. Theodore George Klumpp, president, Winthrop-Stearns, Inc., New York.

Dr. Hugh Rodman Leavall, professor of public health practice, Harvard School of Public Health, Boston.

Dr. Basil C. McLean, professor of hospital administration, University of Rochester, New York.

Dr. James Roscoe Miller, president of Northwestern University, Chicago.

Dr. Milton C. Winternitz, chairman, division of medical sciences of National Research Council, New Haven, Conn.

Dr. Otto W. Brandhorst, dean of Washington University School of Dentistry, St. Louis.

The task force will study operations of all federal medical programs, including Veterans Administration and military, and will recommend possible consolidations. Officially the commission is known as the Commission on Organization of the Executive Branch of the Government. The first Hoover Commission proposed, among other medical changes, that all federal medical services be grouped under a United Medical Administration. The plan was defeated in Congress. The Hoover Commission medical task force has decided to do some of its work in Chicago but most of it in Washington. At its organization meeting, the force decided to meet in Washington every two weeks until the survey of federal medical programs has been completed.

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FOREIGN LETTERS

BRAZIL

Total Gastrectomy.—Among the reasons for the increase of the survival time in recent reports on cancer of the body and cardial regions of the stomach as well as infiltrating tumors of the whole stomach, total gastrectomy is frequently referred to. While some distinguished surgeons in recent papers suggest the routine use of total gastrectomy for the treatment of all cases of cancer of the stomach, other practitioners, no less prominent, oppose this radical procedure. In a recent paper published in *Medicina-cirurgia-farmacia* (17:175, 1953), Dr. Fernando Paulino, head surgeon of the Rio de Janeiro Casa de Saude São Miguel, reports his personal experience in 20 cases in which total gastrectomy was performed in the four and a half years ended on Dec. 31, 1952, in this small and well-equipped hospital. All the 20 patients left the hospital in good general condition and tolerating well the prescribed diet. In all cases the malignancy of the lesions was ascertained by pathological examination. There were 16 men and 4 women, with the minimum age of 32 and the maximum of 72, the average age being 56. The resection involved, besides the stomach, the spleen in 16 cases, the lower third of the esophagus in 6, the pancreas in 3, the colon and the gall-bladder in 2, and the adrenal in one. A solution of glucose, amino acids, and alcohol was used to administer fluids, proteins, and calories needed during the first three days after the operation. Oral feeding was used after the third day, which seems to improve the recuperation of the patients and has no ill effect on the healing of the anastomosis. In no case was a catheter used through the anastomosis. Of the 20 patients, 7 died of metastases within 10 months after the operation, 2 within 24 months, and one after 25 months. One patient was operated on eight months after the total gastrectomy, metastases having been then found involving the pre-aortic lymph nodes. This patient was not seen afterwards for follow-up. Among the nine patients still alive, one was still surviving two years and six months after the operation, one at one year and four months, and seven at less than 10 months.

Dr. Paulino says that his experience does not permit him to recommend total gastrectomy as routine treatment of early gastric carcinomas or of the pyloric region. These tumors should be treated by subtotal gastrectomy, with resection of the great and lesser omenta, four-fifths of the stomach, and 3 to 5 cm. of the duodenum. He thinks that total gastrectomy should be performed in cases of (1) carcinoma of the median part of the stomach; (2) carcinoma of the cardial region of the stomach; (3) carcinoma invading the whole stomach; (4) sarcoma of the stomach of any localization or histological type (such as leiomyosarcoma or lymphosarcoma). He points out that the indication for total gastrectomy in cases of non-malignant lesions must be exceptional; polyposis gastrica seems to him the most legitimate case.

Spraying of Houses with DDT for Control of Leishmaniasis.—During the first trimester of 1947, Dr. F. Nery Guimarães, of the Rio de Janeiro Oswaldo Cruz Institute, studied an epidemic of mucocutaneous leishmaniasis in Suruí, a rural locality of the county of Magé, state of Rio de Janeiro, known as an endemic focus of the disease. Of 306 persons examined, 39 (12.7%) were found to have leishmaniasis on the basis of the presence of the parasite or the positivity of Montenegro's reaction. Also found were 24 persons with old scars suspected to be sequelae of leishmaniasis, this having been later confirmed by the intradermal test. In 12 houses, 136 sandflies (11.3 per house) were collected by hand, all of the species Phlebotomus intermedius; this species was also found, besides several sylvatic species, in the vicinity of the dwellings and the forest. Throughout the surveyed area, from the end of 1947 on, the Serviço Nacional de Malaria has sprayed all houses with chlorophenothane (DDT), at six month intervals. In 1953, after five years of this mosquito control work, at the same season the previous leishmania survey was performed, Dr. Guimarães and Dr. Fernado M. Bustamante, of the Servico de Malaria, carried out a new clinical and epidemiological investigation that will be described in a future issue of the *Revista Brasileira de Malariologia*. Following is a summary of their findings:

In a house to house canvass, only one (0.3%) of 296 persons in 74 dwellings was found to have leishmaniasis. Sandflies were searched for by hand in the interior of several houses, including the 12 from which numerous specimens had been captured during the first survey. The results were entirely negative. New captures were then performed, this time by means of spraying an insecticide with a pyrethrum basis (Flytox) through a manual pump. Ninety-four houses were inspected, all having been sprayed except 20 that were uninhabited or closed at the moment. These 94 houses represented almost all of the community. The spraying of each house, done at the first hours of the evening, lasted an average of 20 minutes, and, at the end, a careful search was made for the insects. No sandfly was found inside the dwellings. In the outside—near the living areas and in the forest—manual captures were made, and, as had occurred before the DDT spraying of the region, many sandflies were collected, a part of them Phlebotomus intermedius, i. e., the same species found before in the interior of the houses.

As ascertained by the authors, the leishmania case rate fell from 12.7% to 0.3% after the regular chlorophenothane spraying of the houses. Since about 50% of the persons infected with leishmaniasis found before the spraying were treated thereafter, this may have been a factor in limiting the normal spread of the disease, but this could never explain the almost total disappearance of the disease, which is undoubtedly the result of the absence of sandflies in the dwellings. On the other hand, as these insects are still found outdoors, the extradomiciliary transmission of the disease should have had only a secondary role in the increase of the intensity of the focus. This means that the disease was, at the time of the former investigation in this area, spread predominantly in the houses, thus explaining its epidemic character. The presence of a considerable number of sandflies so near the houses, but not in their interior, added to the fact that they belonged to a semidomiciliary species, i. e., Phlebotomus intermedius already found before in the interior of the dwellings suggests that chlorophenothane not only kills the flies but repels them. To explain a different result reported by Corradetti in 1952 of the disappearance of sandflies not only from the interior of the houses but also from their vicinity after two chlorophenothane sprayings, the authors emphasize the fact that the sandflies of the region studied (Abruzzo, Italy) are only domiciliary, and apparently breed in the neighborhood of the dwellings, feeding on man and domestic animals exclusively. Since in this case the stables had also been sprayed and there are almost no forests there (and consequently not enough wild mammals), the flies had almost no source of food and disappeared entirely.

The disappearance of the sandflies from the interior of the houses causing the sharp decrease of leishmaniasis to an insignificant level, as observed in the focus under study, enables the authors to predict a similar result in all regions in which leishmaniasis is endemic (the visceral form as well) and where a campaign of domiciliary DDT spraying will be carried out. Therefore, they recommend this method as a basis for leishmaniasis control.

The items in these letters are contributed by regular correspondents in the various foreign countries.

Congenital Absence of Gallbladder.—Excluding patients in whom there were also other malformations of the biliary ducts, only about 75 patients with congenital absence of the gallbladder have been reported in the medical literature. Dr. Luis da Costa Lima, of the Rio de Janiero Hospital dos Pescadores, recently reported three more cases in *Rivista Brasileira de Cirurgia* (**25**:179, 1953). In these patients, two women and one man, icterus was the most prominent symptom, and the correct diagnosis was made only during the operation, as was the case in the patients previously reported. In two of these patients a diagnosis of stone obstructing the ductus choledochus was made, and in the third, the biliary peritonitis was recognized but the diagnosis of vesicular agenesia was not made. In this patient the biliary peritonitis was probably caused by retroduodenal perforation of the ductus choledochus, because inspection of the subhepatic space revealed a flow of small calculi through the epiploic foramen. Therefore, the so-called choleperitoneum without perforation (which was admitted by Buchanan as possible after edema of the extrahepatic biliary ducts, imperceptible rupture of the biliary ducts, or a retroperitoneal biliary flooding), did not occur. According to Mariano de Andrade, who published a report on a patient with congenital absence of gallbladder associated with choleperitoneum in 1949 in Brazil, this condition is extremely rare, since he did not know of another case in the medical literature before his own. The author's case would then be the second of the kind, and probably the first with a clear rupture of the ductus choledochus. The author points out that in his first patient the fossa vesicae felleae was present but empty, and reminds us that, according to Dixon and Lichtman, the fossa vesicae felleae was present in only 7 of 90 patients with vesicular agenesia of all kinds.

Vesicular agenesia has no symptomatology of its own, but abnormalities of the biliary ducts are common in connection with this condition. The ductus choledochus may or may not be dilated even in the absence of stones. In the three patients reported the duct was greatly dilated and contained several stones. In one patient stones were also present in the left hepatic duct. As vesicular agenesia is a condition with symptoms similar to those of lithiasis of the ductus choledochus, especially if accompanied by icterus, the author suggests that, during the operation, the ductus and the adjacent organs should be examined and, if possible, cholangiography with retrograde filling should be performed.

DENMARK

Chemotherapy of Tuberculosis.—Prof. K. A. Jensen and his co-workers have reported that, in cases of pulmonary tuberculosis with cavitation, the administration of isoniazid may produce resistant strains of tubercle bacilli after only two weeks. After three months of treatment with this drug, about 88% of the organisms have become resistant to it. Indeed, when isoniazid is given by itself resistance to it develops almost as quickly as it does to streptomycin. In one series of patients combined treatment with isoniazid and *p*-aminosalicylic acid was given with the result that after three months a tendency to a rise of resistant strains of tubercle bacilli was demonstrable in only 2 out of 13 patients. A month later, 3 of these 13 patients showed isoniazid-resistant strains. The most effective treatment was found to be a combination of streptomycin, *p*-aminosalicylic acid, and isoniazid. The addition of isoniazid to the combination of streptomycin and *p*-aminosalicylic acid did not give rise to any greater discomfort in the patient. At present, treatment with isoniazid alone should be avoided, however tempting it may be to give it at home and without any serious inconvenience. The optimal dosage of the three drugs is being investigated, and it already appears that an appreciable reduction can be made in the dosage of streptomycin without seriously impairing its therapeutic action. Although at one time as much as 3 gm. of streptomycin was given daily, only 1 gm. weekly need be given when it is combined with *p*-aminosalicylic acid and isoniazid.

Sexual Life of Young Danish Women.—Dr. Kirsten Auken, who is the mother of five children, has written a book on the sexual life of women between the ages of 20 and 35. Her material was obtained from three hospitals in different parts of Denmark. She interviewed the patients only when they were about to leave the hospital in order to avoid undesirable gossip in the hospital itself. The physicians in charge of two other hospitals refused their consent to these interviews that were granted with such unanimity by the patients that only 3 out of 318 women refused to partake in them. It was perhaps inevitable that Dr. Auken's work should promptly be called a Danish Kinsey report, but she insists that her methods and findings differ from those of Dr. Kinsey. Her material was gathered from every social class and from many different parts of Denmark. She found that the lower the social class, the earlier the age at which sexual relationships are started, and her findings suggest that the homosexual rate among Danish women is much lower than that discovered by Kinsey in the United States. With regard to the source of information about sexual matters, other women were responsible in 46% and the mother imparted this knowledge in 11.9%; 52% of the women wished that they had been better informed on the subject. In 8.8% sex information was obtained by observing the behavior of animals. Sisters had imparted sex information to another 8.8%, but only 3.1% had been given sex education in school. Respectable publications on the subject had been the main service of information for 5.1%, and pornographic publications for only 1.7%. Many woman, 88.6%, wanted for their children a more adequate sexual education than they themselves had had.

Drug Addiction Problems.—At a meeting of the Copenhagen Medical Society, the problems of drug addiction were discussed. Some of these problems may seem insoluble, but their discussion from time to time helps not only to give a fairly accurate impression of their scope but also to indicate new means that may prove helpful. One speaker referred to a comprehensive analysis he had recently undertaken of about 54,000 medical prescriptions that in the course of a month had been filled by retail druggists. Morphine and opium were numerically the most important drugs prescribed. Amphetamine came next, and meperidine (Demerol) hydrochloride and methadone (Butalgin) hydrochlirode were less popular. Although 40% of the narcotic prescriptions were for morphine or opium, only 2% were for heroin and 2% for cocaine. As was to be expected, many of the prescriptions had been refilled frequently for the same person. The speaker emphasized the practical value of keeping an index file of addicts in Denmark. Another speaker suggested that it should be made illegal to be found in possession of narcotic drugs without a sound reason for it. At present it is only when such drugs are acquired by theft or forgery that their possessors can be prosecuted. If the mere possession of them without justification could be made a criminal offense, it might be possible to prevent addiction in some narcotic users. Another speaker referred to ships' medicine chests as a serious loophole through which narcotics can be obtained. At present any ship's captain can order a supply of such drugs without a physician's prescription. Yet another speaker reported that 56 of 80 patients admitted to hospitals for drug addiction between 1944 and 1950 represented readmissions.

LONDON

Reports on National Health Service.—A detailed account of the working of the National Health Service in England and Wales in 1952 shows a net expenditure for the year ended March 31, 1952, of £348,457,732. At the end of 1952 the number of beds in hospitals was 507,368. The number of inpatients (measured by discharges and including deaths) during the year was 3,414,373, compared with 3,259,214 in 1951. The number of new outpatients increased by 4.9% to 6,605,765. The total waiting list increased by 527 to 500,307. The waiting list for tuberculous patients fell from 7,096 to 6,126. At the end of the year there were 63 mass radiography units in civilian use. In these units 10,654,554 persons had been examined, of whom 3.3 in every thousand were found to have active tuberculosis. Up to the end of the year, about 93,600 persons had been vaccinated with BCG. This figure

includes, in addition to contacts, nurses and medical students because of their greater than average exposure.

During the year surgical and medical appliances were provided through the hospital service to the value of £2,980,000. These included 44,991 pairs of surgical footwear, 75,393 abdominal appliances, 35,373 elastic stockings, and 7,255 wigs. The number of new artificial limbs (including replacements) provided since the service began rose from 40,217 to 51,250. The number of invalid chairs and tricycles provided during the year was 12,411, and 7,369 artificial eyes were provided. Hearing aids were supplied to 88,000 new patients, bringing the total supplied since the beginning of the service to 260,000. There was still a wainting list of 66,000.

The total number of blood donations was 647,009, the highest total in any year since 1944, the peak year of the war period. An analysis of how blood was used was made on a 5,000-bottle sample in an industrial city, with the following results: accident cases 10.45%, gynecologic and obstetric patients 19.67%, medical patients 32.23%, and surgical patients 37.65%.

In 1952, the x-ray departments of about 600 hospitals (about half the hospitals with such facilities) carried out 741,000 examinations of patients referred directly by general practitioners. The comment was made that "where the service is available it is certainly not abused and the demand has been less than anticipated." During the year 400 hospital pathology laboratories (just over half the total number in the country) dealt with 554,000 specimens that had been referred directly by general practitioners.

A detailed analysis of general medical practice within the service as of July 1, 1952, showed that there were 17,204 physicians providing unrestricted general medical services, of whom more than half were practicing in partnership with one or more other physicians. There were also 1,689 "permanent" assistants (assistants employed for periods of three or more months) and 309 assistants in training. Twenty-two per cent of the physicians practiced in rural areas, 34% in semiurban areas, and 44% in urban areas. The geographical distribution of general practitioners shows that the towns having fewest physicians per unit population are those in the industrial Midlands, on the north-east coast, in South Yorkshire, and in Lancashire. The areas with the smallest average lists of patients were in the southern half of England, North Wales, and seaside towns. There is a tendency for proportionately more of the physicians in the "under-doctored" areas to be in younger age-groups.

Since the introduction of the National Health Service there has been much talk about the difficulty in assistants in general practice getting practices of their own or in becoming partners. This survey shows that, of 1,689 assistants employed in July, 1952, more than half were employed by physicians practicing alone. Ninety per cent of them were the sole assistants employed by the medical firm in which they were working. Two-thirds of them were aged 35 or under, and most of these had been in their present posts for less than two years; one-fifth of the total were aged 36 or over and had been in their present posts for over two years, and 14% were aged 46 or over. During the second half of the year 51 assistants became principals and 131 became partners in existing practices. Of these, one-half had been assistants for less than a year; a quarter for one or two years; one-eighth for two to three years; and the remainder for longer periods.

During the year 412 alleged breaches by general practitioners of their terms of service were considered by service committees and reported to the ministry by executive councils. In 251 cases the council recommended that no action be taken. In 47 a warning letter was sent, and in the others some action was taken, usually consisting of the withholding of money.

Caution Concerning Cortisone.—A note of caution concerning the use of cortisone in the treatment of rheumatoid arthritis was struck by two of the contributors to the annual symposium on advances in treatment in *The Practitioner* (**171**:346-425 [Oct.] 1953). Prof. D. M. Dunlop of the University of Edinburgh stated: "Although hypercortisonism modifies the reaction of the host to certain agents, it has little or no effect upon the agent itself. In . . . rheumatoid arthritis, the noxious etiological agent may persist indefinitely, and a return of signs and symptoms following withdrawal of the hormone almost invariably ensues. This 'rebound' phenomenon often occurs in a peculiarly virulent form. In such disorders therefore, to effect suppression of the manifestations of the disease, the hormone has to be given indefinitely. The suppressive dose is seldom less than 50 or 75 mg. a day, and unfortunately few patients can be adequately controlled for long periods of time on such doses without eventually developing the undesirable side-effects of hypercortisonism which will necessitate abandonment of treatment. Further, the dose of cortisone adequate to suppress symptoms tends to rise in the course of time and the dangers of sodium retention, oedema and hypertension become greater with advancing years. Prolonged treatment is liable to cause osteoporosis, sometimes manifested by the sudden collapse of a vertebra. Thus, the longer an induced hypercortisonism is sustained, the more are injurious side-effects likely to be encountered. In these circumstances the ethics of relieving symptoms temporarily with cortisone must be seriously questioned in any patient in whom the noxious etiological agent is likely to persist permanently. Indeed, in rheumatoid arthritis there is some evidence that in the long run the ultimate state of patients controlled by cortisone is no better than those controlled by adequate doses of aspirin."

A similar attitude was adopted by Dr. William Tegner, London Hospital, who said, "The advocacy of these new [agents] . . . has led to enthusiastic trial [which] . . . must be expected so long as rheumatoid arthritis remains a disease of unknown etiology and doubtful prognosis. Both doctor and patient are quite naturally eager to clutch at straws . . . But after early hope and optimism, disappointment inevitably follows. . . . Cortisone and ACTH can have a profound and gratifying effect in suppressing the activity of rheumatoid arthritis but . . . this early effect may need progressively larger doses for its maintenance and . . . prolonged treatment may bring with it a host of difficult and even dangerous side-effects. . . . It has been suggested that the rôle of cortisone and ACTH is to tide the patient over until a natural remission has set in; but one can never foresee when a remission will occur and too often dangerous side-effects have become apparent before any remission has manifested itself. These difficulties are especially prominent in elderly patients and in post-menopausal women, who seem to tolerate prolonged treatment with these hormones very badly."

Potassium Permanganate as an Abortifacient.—Five new cases of vaginal ulceration following the insertion of potassium permanganate for the purpose of procuring abortion were reported by E. A. J. Almett and C. S. Nicol (*Brit. M. J.* **2**:759, 1953). Three had vaginal bleeding, one a brownish vaginal discharge, and one pain, dysuria, and swelling of the vulva. Four of the patients were found to have the characteristic apposition vaginal ulcers produced by potassium permanganate. Four gave a history of inserting tablets to achieve abortion; the remaining one admitted only using a solution of tablets in a douche. Bleeding occurred in all five, but in none was packing or transfusion necessary, although ligation of a bleeding artery was necessary in one. Abortion as a result of the use of the tablets did not occur in any of the patients. Three first attended a gynecologic outpatient department, and two a venereal diseases clinic. The main difficulty in diagnosis is confusion with primary syphilis, as the ulcers may be mistaken for contact chancers. The common use by women of potassium permanganate in tablet form for procuring abortion and the ease with which it may be obtained were stressed. Tablets of potassium permanganate are readily obtainable from pharmacists, and there is no restriction on their sale.

New Developments in Radiotherapy.—News has just been released of the installation of a linear accelerator and a cyclotron in the Medical Research Council Radiotherapeutic Unit at Hammersmith Hospital. The radiotherapeutic unit

occupies the end wings and three stories of the central block. The two-story north wing houses a 45-in. cyclotron, and the single-story south wing houses an 8 mev linear accelerator. The fourth floor of the central block is occupied by a hospital research department. Four more stories of the central block (yet to be built) will be occupied by the London University Postgraduate Medical School. Each wing was designed as a self-contained unit to be linked up with the central block containing laboratories. The cyclotron suite was planned to go above ground and not below ground as is sometimes done to provide protection against radiation. In the case of both the cyclotron and the linear accelerator protection is provided by reinforced concrete walls and roofs about 6 ft. thick. The main doorway to the cyclotron chamber is formed with an electrically operated 35-ton door consisting of a steel box filled with concrete. The door between the cyclotron chamber and the assembly bay is a 190-ton electrically operated, horizontally moving door of reinforced concrete.

The linear accelerator is a direct descendant of radar, and provides another example of wartime discoveries being applied to medicine. It has been developed by the Atomic Energy Research Establishment in colaboration with the Medical Research Council Radiotherapeutic Unit and makes use of the frequency magnetron that is the basis of radar. It receives its name from the fact that it accelerates a beam of electrons down a straight tube (3 m. in length), and in this process a voltage of 8 million is attained. The beam has a very short wave length and a relatively great penetrating power, and it is hoped that it may prove of value in the treatment of deep-seated malignant growths. From the point of view of handling, it is as compact and as easily handled as the ordinary deep x-ray units of 200,000 volts now in general use. The one that has been installed at Hammersmith is the first of its kind to be used for clinical purposes, and the results of its use are awaited with much interest. It is reported that the Ministry of Health has already placed orders for several 4-million volt units for installation in various hospitals throughout the country.

The cyclotron, which is still in the process of construction, is the first cyclotron in this country to be built in a hospital. Its potentialities in medicine are still not clearly defined, but two uses are immediately indicated. One is for the production of radioactive isotopes of such a short life that they can be used only for therapeutic or research purposes. The other is to determine whether the neutron radiation of the cyclotron has any advantages over other forms of radiotherapy in the treatment of malignant disease.

The Physician's Office.—Within a fortnight of the publication of the report of the British Medical Association committee on general practice, a letter was sent by the general medical services committee of the British Medical Association to every general practitioner in the National Health Service, "earnestly hoping that [he] will do his utmost to provide the highest possible standard of surgery and wainting-room accommodation for his patients." The opinion is expressed that the general standard is of a high order, but "a number of general practitioners have, by reason of building restrictions and the high cost of repairs and maintenance, been prevented from doing all that they would have wished in this respect." It is pointed out that under his terms of service a practitioner at his own expense "is required to provide proper and sufficient surgery and wainting-room accommodation for his patients" and that any member or officer of the executive council or local medical committee can, under the regulations, inspect the accommodation provided. Further, a practitioner's remuneration in the National Health Service takes into account his obligations to provide suitable premises, and it remains his personal responsibility to provide them at his own expense.

Physicians should review the surgery and wainting room accommodation in their practices for the following reasons: 1. There has been a general relaxation in building restrictions. 2. Health centers are unlikely to be built on a large scale for a long time to come. 3. As a result of the Danckwerts award, general practitioners are in a better position to embark on such expenditure. 4. The practice expenses ratio established by the Danckwerts award includes a substantial element in respect of the cost of maintaining surgery premises. The committee does not consider it either practicable or desirable to lay down any minimum standards. It believes that any necessary improvement in the standard of accommodation provided should develop spontaneously from a wish by the physicians concerned to ensure that their offices are compatible with the prestige and status of general practice in the service.

SWITZERLAND

International Congress of Rheumatic Diseases.—The Eighth International Congress of Rheumatic Disease was held in Geneva Aug. 24-28. Over 1,000 rheumatologists from about 40 different countries, including the U. S. S. R., attended. The welcoming address was delivered by Prof. K. M. Walthard, president of the organizing committee. Dr. Knutti, of the National Institute of Arthritis and Metabolic Diseases, Bethesda, Md., told of the fight against rheumatic diseases in the United States. A series of reports was devoted to the study of the relations between rheumatism and conjunctival tissue. Professor Nesterow of Moscow expounded the theory that rheumatism is an infectious-neurogenic reaction in which disturbances in the floor of the diencephalic neurovegetative centers play a large part. Professor Reichstein, from Basle, spoke on the chemistry of hormones of the adrenal gland, and especially hydrocortisone (17-hydroxycorticosterone) and desoxycorticosterone. His synthesis of these hormones a few years ago brought him the Nobel prize in medicine. He then announced the discovery of a new compound provisionally named electrocortine. This substance is closely related to desoxycorticosterone and its physiological and pharmacological action is said to be 30 to 40 times more powerful. Its place in the treatment of rheumatic diseases has not yet been definitely determined. Dr. Philip Hench, from the Mayo Clinic, reported on the therapeutic use of cortisone and corticotropin (ACTH) in rheumatism. He warned against the abuses of cortisone, described the prevention and the treatment of hypercorticism, the methods of interruption of the treatment, and the prevention of acute adrenal insufficiency in patients treated by these hormones who might have an increased reaction to stress as a result of a serious infection, a trauma, or a surgical operation. Professor Goslings set forth the criteria needed to evaluate the degree of action of a preparation of corticotropin in man. This study showed the difficulties of testing the activity of this hormone and the necessity, during a clinical study, to use a single source of hormone.

These five days of scientific work were pleasantly interrupted on Aug. 26 by a journey to Aix-les-Bains, the well-known French center for the treatment of rheumatism, where clinics were held for the visitors. As the scientific sessions continued, the two protagonists of the introduction of plastic material for the reconstruction of diseased femoral heads, Prof. Merle d'Aubigné and Dr. Judet, of Paris, presented the results of seven years of experience. In a series of 500 cases of coxitis, Dr. Judet observed good results that have been maintained for several years in 65% of patients. Many of these patients who had been invalids were enabled to walk and some even to return to their work. Because of the tendency to remissions and the progressive nature of polyarthritis, the rehabilitation of patients is difficult. Bennett, of the International Labour Office in Geneva, spoke of the efforts of this organization to find for the patient employment best adapted to his remaining abilities.

Prof. Maurice Roch Retires.—Prof. Maurice Roch, who has reached the age limit for teaching, will leave the faculty of medicine of Geneva University in October. He will be remembered for his book "Dialogues Cliniques" and for his approach to the patient as an individual rather than as a specimen. Professor Bickel, a disciple of Professor Roch, will succeed him.

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1953

CORRESPONDENCE

THE KINSEY REPORT

To the Editor:—The newer findings concerning physiology of the pubococcygeus muscle strike at the very roots of the conclusions implied by the Kinsey report. Even if the statistical data were unassailable, Kinsey's interpretation is based on concepts that have long been controversial. This applies particularly to the question of vaginal and clitoral orgasm. I believe, as many others do, that research in the physiology of the pubococcygeus muscle has produced overwhelming evidence in favor of the existence and importance of vaginal orgasm.

Kinsey stresses the subject of conditioning, especially in relation to premarital experience. Obviously, if conditioning emphasizes clitoral stimulation, the problem of future satisfactory sex relations is aggravated. I believe, if this fundamental error in Kinsey's understanding of orgasm is adequately exposed, considerable doubt will be thrown on the accuracy of his conclusions. The necessity for mitigating the impact of the Kinsey report on the public is illustrated by a recent radio discussion on juvenile delinquency. Judge Bernstein of Los Angeles stated that it has become difficult to answer delinquent girls who brazenly quote the Kinsey report in order to justify their actions. Similar observations have come from probation officers. A former president of the California Bar Association remarked that judges are looking for well-founded medical opinions to counter the irresponsible use of the Kinsey report.

Parents find themselves in the same dilemma, and they will appreciate well-presented physiological knowledge that will help them guide their children. It is possible that many youngsters, who do not understand the importance of moral and legal restraints, may accept the advisability of avoiding behaviors that are detrimental to their future sex appreciation, happiness, childbearing functions, and prevention of so-called "female complaints."

Now as to Kinsey's book. For the stated purpose of his research, i. e., establishment of a basis for the revision of existing sex laws, Kinsey applied the statistical method, which is widely accepted in the social sciences. This is not the place to go into the question of whether material gathered by that technique is significant from the medical point of view. We must, however, take cognizance of the fact that histories based on interviews were collected during a 15 year period prior to Jan. 1, 1950. It appears that the standardized questions were formulated on the basis of information available at onset of the inquiry, approximately 18 years ago.

With regard to the anatomy of the pubococcygeus muscle and the sexual physiology of the vagina, the decisive discoveries were published only subsequent to that time. In February, 1939, Curtis, Anson, and McVay presented (in *Surg, Gynec. & Obst.*) completely new findings concerning the anatomy of the pubococcygeus muscle. In particular, Anson demonstrated the presence of minute terminal interdigitating fibers inserting in the wall of the urethra and of the middle third of the vagina. Anson stated that all previous descriptions of pelvic anatomy are either incomplete or erroneous. Anson's work on the pelvic anatomy became more readily accessible in the fifth edition of Curtis' "Textbook of Gynecology" (1947) and subsequently in Anson's "Human Anatomy" (1950). Kinsey's statements are based on the assumption that the vagina is insensitive because its superficial tissues contain few if any sensory nerves; on the other hand, his material indicates that satisfaction is, in a certain percentage of cases, obtained from vaginal penetration during coitus. He assumes the presence of a "mechanism that lies outside of the vaginal walls themselves" (page 581). Kinsey states further "that the deep penetration of the rectum may bring satisfaction which is, in many respects, comparable to that which may be obtained from a deep vaginal insertion" (page 581). His report that anal and deep vaginal feeling are parallel can be explained by the anatomic arrangement of the pubococcygeus, which surrounds both organs. My clinical studies have led me to conclude that within the pubococcygeus there exist highly specialized proprioceptive nerve endings. Any sensation received by these proprioceptors must differ from that derived from superficial innervation.

The pubococcygeus varies widely in different women, independent of age or childbearing. Roughly speaking, one-third of all women have a strong pubococcygeus, another third have a weak and atrophic pubococcygeus, while the rest can be described as borderline cases. The status of the pubococcygeus shows a definite relationship to the various functions of the muscle, i. e., support, stretching during parturition with subsequent return to normal, bladder control, and sexual response.

It is interesting to refer to a paper by John W. Huffman (The Effect of Gynecologic Surgery on Sexual Reactions, *Am. J. Obst. & Gynec.* **59**:915-917 [April] 1950). who found that various gynecologic operations, including removal of the clitoris, did not interfere with sexual activity in mature women. Huffman states: "This study would tend to bear out the assumption that the vagina becomes the center of normal sexual activity in the mature female. . . . Sexual stimulation increases engorgement of the genitals; as a result of physical contact vaginal sensory organs are stimulated. These stimuli produce vaginal contractions and spasmodic muscular movements which culminate in a phenomenon comparable to the male orgasm, but without the discharge of retained secretions."

Kinsey remarks, on page 580, "The relative unimportance of the vagina as a center of erotic stimulation is further attested by the fact that relatively few females masturbate by making deep vaginal insertions." This statement is significant, as Kinsey consistently uses response to masturbation as the measuring stick of orgasm. Of further interest are the figures in table 23 (page 178) concerning the incidence of masturbation in married women. The figures lie between 23 and 36%, with a rough weighted average of 33%. It is noteworthy that examination of many thousands of women has shown that the pubococcygeus is weak in about one-third of them. It is my impression that the same third masturbate during married life, because weakness of the pubococcygeus renders them unable to receive sexual satisfaction from coitus. Many of our patients abandoned clitoric stimulation and masturbation as soon as function of the pubococcygeus was improved.

I have found that women who depend on clitorolabial stimulation are as a rule not aware of the presence of the pubococcygeus and of the possibility of contractions of this muscle. In the restoration of function of the pubococcygeus, it is of decisive importance that awareness of the muscle be established as a first step. In several publications I have stressed this point. A surprising finding is that mere awareness of the pubococcygeus and its contractility tends to improve its various functions. This applies also to sexual appreciation, which may thus be enhanced even before active exercises are instituted. In many women with borderline problems of lack of disturbance of vaginal feeling, it is sufficient to identify the pubococcygeus for the patient and to inform her of its contractile and sensory potentialities. Concentration on the muscle seems to cause patients in this group to forget the clitoris.

Naturally, the question must arise as to why the pubococcygeus shows such great variations in women. It should be mentioned that, among the thousands of women examined at Los Angeles County General Hospital and in private practice, there were women from various races and extractions, including Negroes, Mexicans, Chinese, and others. No differences could be established on the basis of national or racial origin. The explanation must, therefore, be looked for in the phylogenetic character of the pubococcygeus. The former "tail-wagger" lost its principal means of exercise when the human being assumed the upright position, while at the same time a new function, pelvic support, was added. The pubococcygeus, along with the quadriceps and rectus abdominis, is an old muscle in transition, prone to atrophy of disuse. It must be maintained in a state of tone and vitality through conditioned reflexes.

Seventy-five per cent of women with urinary stress incontinence during adult life present a history of difficulties with micturition in childhood. This finding indicates that the development of a strong pubococcygeus is related to training in sphincteric control, both anal and urinary. The sexual function of the pubococcygeus is superimposed on these sphincteric and supportive functions acquired earlier. It is very improbable that vaginal feeling can be established in a poorly developed pubococcygeus at the time of first intercourse, be it gentle or rough; but subsequently the sexual function may be developed in some cases. The response of a strong pubococcygeus to the quality of first intercourse is not consistent. In some women sexual conditioning is brought on in spite of a rough first experience, but as a rule a gentle, gradual technique is more conducive.

Kinsey stresses premarital experience as important for sexual appreciation, without reference to the quality of early experience. In view of the physiological facts concerning the pubococcygeus muscle, Kinsey has missed the most important point completely. The effect of early experience depends on the factors associated with coitus as an expression of true love, which Kinsey ignores throughout his book. A first experience, whether marital or premarital, that begins with rape and fear and under uncomfortable or immoral circumstances is hardly conducive to conditioning of the highly sensitive vaginal function. Conditioning of response exclusively to clitoral stimulation interferes with the development of vaginal feeling.

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ATRIUM AND AURICLE

To the Editor:—It is extremely gratifying, at long last, to note that "official" recognition has been given to the general misuse of the word auricle in well-known clinical entities such as atrial flutter, atrial fibrillation, atrial septal defects, and atrioventricular block. The recent (fifth edition, 1953) "Nomenclature and Criteria for Diagnosis of the Heart and Blood Vessels" published by the New York Heart Association and distributed by the American Heart Association has finally discarded auricle for atrium wherever the upper chambers of the heart are concerned. This is a delayed but welcome concept that has been ignored in previous editions of this valuable manual.

About 25 years ago I joined with the late Dr. A. E. Parsonnet in an endeavor to correct the traditional misuse of the word auricle in describing the atria of the heart. Our objections were based on the very definition of the word: "Auricle [L. auricula, the external ear]. 1. The pinna of the ear; the ear flap or external ear. . . . 2. An appendage to the atria of the heart; auricular appendix. 3. Any ear-shaped structure or appendage. 4. Commonly used mistakenly for atrium" ("Blakiston's New Gould Medical Dictionary," Philadelphia, the Blakiston Company, 1950, p. 109). In a previous communication ("Discarding of Out-Dated Medical Terms," *J. A. M. A.* [July 5] 1952) I originally included the word auricle in the list of medical terms that had out-lived their initial concept, but it was omitted in favor of such old time favorites as water hammer pulse and hobnail liver. There appeared to be a general reluctance among most clinicians to abandon a word as familiar as auricle, although its misuse was well recognized by all teachers of medicine.

The more or less rapid change from auricle to atrium in medical thinking during the past few years has been due chiefly, I believe, to the advances made in cardiac surgery. On the operating table the auricle is definitely an appendage to the upper chamber of the heart; it is not the entire chamber. As a technical procedure it became necessary for the surgeon to differentiate the atrium as a whole from the auricle; in mitral commissurotomy the left auricle is sometimes amputated and removed. This surgery would be impossible under the traditional use of the word.

The obvious purpose of this communication is to point out the need for a prompt acceptance of the word atrium in place of auricle in all future medical literature. The words are no longer colloquially interchangeable. The auricle, insofar as the term refers to the heart, is an appendage to the atrium. The terms auricular flutter, auricular fibrillation, and the like no longer serve any useful purpose.

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QUININE IN TONIC WATER

To the Editor:—Cinchonism is relatively rare in the United States both because of the low incidence of malaria and because of the use of the newer antimalarial drugs when indicated. I think it worth while to present to your readers the following unusual reaction because of the increase in popularity, at least in the east, of the drink "gin and tonic."

I saw a 43-year-old man in consultation who had a seven week history of tinnitus and hearing loss. He had consulted an otologist, who found bilateral diminution in hearing, and a neurologist, who suggested the diagnosis of bilateral angle meningioma. Because of the history of daily ingestion of seven to eight drinks per day he was sent for a medical evaluation prior to further workup for neurosurgery. The history of alcohol ingestion was correct, but his diet was in general adequate. After a physical examination, which was not remarkable except for the facts already noted, casual discussion brought out the fact that the drinks were always gin and tonic. Since I had seen cinchonism in the southwest Pacific, I thought it worth while to change the beverage to Tom Collins. Within 48 hours the symptoms had disappeared. A test dose of 300 mg. of quinine brought a return of the tinnitus. Later, a test dose of 150 mg. produced the same effect. Three weeks after the discontinuance of the quinine, audiogram showed restoration of hearing.

While I have not obtained the exact formula of quinine water, I am informed that the Schweppes brand contains about 30 mg. per pint. The man was ingesting about 100 mg. daily. It is clear that it would take an enormous consumption to produce the symptoms in the normal adult, but the existence of idiosyncrasy is well known, and this source of supply seems, therefore, worth publicizing.

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COUNCIL ON INDUSTRIAL HEALTH

This report is endorsed by the Committee on Occupational Dermatoses of the Council on Industrial Health. The Council has approved publication.

C. M. PETERSON, M.D., *Secretary.*

CHROMATE HAZARDS IN INDUSTRY

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The element chronium was identified in 1797. Within 30 years, chromium compounds were mentioned in the medical literature as a cause of ulcerations and dermatitis in the workers who used them.[1] Today chromium and its salts are widely used in industry and are being used in ever-increasing amounts. The purpose of this paper is to mention some of the important industrial uses of chromium and to discuss the medical problems of its use, particularly chromate dermatitis.

Chromium and its compounds are obtained from chromite ore, which is a mixture of iron and chromium oxides. It is a gray metal, with a melting point of 1,890 C and great resistance to corrosion. It has valences of 2, 3, and 6 and forms both chromium salts and chromates. The bivalent chromous salts are unstable and of no commercial importance. Chromic oxide (Cr_2O_3), a green pigment, and chromic sulfate ($Cr_2[SO_4]_3$), which is used in tanning, are trivalent chromium compounds. The hexavalent compounds, such as sodium dichromate ($Na_2Cr_2O_7$), are the most active chemically and the most widely used. They probably are the only forms that pose any problem from an industrial health standpoint.

COMMON USES IN INDUSTRY

The following paragraphs consist of a brief discussion of some of the commoner uses of chromium compounds in industry and the various medical complications, such as systemic intoxication, perforated septum, chrome ulcer, and dermatitis, that may arise during such use. These medical aspects, particularly the dermatoses, will be considered in detail later.

Chromium plating for decorative and anticorrosive coatings is an electrolytic process in which metallic chromium is deposited on the cathode from a solution of 20 to 40% chromic acid contained in an open tank. Hydrogen is liberated at the cathode, and the hydrogen bubbles rising to the surface produce a mist of chromic acid. When this mist is inhaled, it first comes in contact with the mucous membrane of the lower nasal septum, sometimes causing ulceration and later perforation.[2] If concentrated mists reach the lungs, acute pulmonary symptoms may result.[3] Recently, possible chronic hepatic intoxication from prolonged inhalation of these mists has been reported.[4] Contact with the mist or solutions will, of course, also cause dermatitis in sensitive persons or high concentrations may even cause a primary irritation. In large scale operations, such as in plating automobile trim, the procedures are almost completely automatic, so that few workers are exposed to the acid. Today proper ventilation and exhaust ducts minimize the danger in most shops. It is in the smaller plating establishments where protective measures are not strictly enforced that trouble occurs. Workmen handle pieces just removed from the chromic acid solution, and frequently the solution is spilled or dripped on the floor. Sweepings from the floor of one small plating shop contained 10% chromium, which would be equivalent to 20% chromic acid. Most workers in the plating industry are familiar with the chrome sore, perforated nasal septum, and chromate dermatitis, and few even consult a physician about the first two conditions. If a chromate dermatitis develops, however, the worker usually must leave the trade, since complete avoidance of contact is difficult because of the contaminated work area.

Anodizing is another electrolytic type of anticorrosive metal treatment, used principally on aluminum. Almost all aluminum airplane parts are so treated. Baths of 5 to 10% chromic acid are used, and the metal to be treated is the anode. An anodic film of aluminum oxide is formed on the metal, which serves as a protective coating in itself or as a base for the application of zinc chromate priming paint. Zinc chromate paint is a common cause of dermatitis in the aircraft industry. The chromic acid mists evolved by the anodizing process are much less concentrated than those formed in chrome plating. Thus, the danger of the occurrence of perforated septum or toxic effects from inhalation is much less, although chrome ulcers and dermatitis have occurred. Other anticorrosive treatments involve only the immersion of metals in baths of various chromate solutions for the formation of anticorrosive films. Dermatitis and possibly chrome ulcers may be encountered but have not been reported in the literature.

In the processing of chromite ore to produce chromium compounds, considerable dust is formed, which contains monochromates and dichromates. While systemic intoxication has not been reported, there seems to be a long-term hazard of carcinoma of the lung from inhalation of this dust.[5] Perforated septums and chrome sores are common in these workers.[6] Dermatitis has been seen infrequently. Dust control measures have been adopted to eliminate the more serious hazard of pulmonary carcinoma.

Despite the fact that the steel and refractory industries use more than 80% of the chromite ore, no instance of dermatitis has been reported among them, since trivalent and metallic chromium apparently are not irritating or sensitizing substances. Chrome steel may contain from 0.5 to 35% chromium. A dermatitis due to chrome steel identification tags has been reported,[7] and chrome-plated metal has been cited as causing chromate dermatitis.[8] These observations were not, however, checked by proper patch testing and are not definitely known to be reactions to metallic chromium or chromate. Refractory grade chromite ore is used to make bricks for the lining of steel furnaces.

Since the early 1930's chromates have been used for the control of corrosion in various types of recirculating water systems. They are so effective in this capacity that their use is standard in diesel railroad locomotives. They are also used in some other internal combustion engines, in refrigeration systems, in the brine in ice plants, and in some air conditioning installations. Their use for the same purpose in oil well mud, gas wells, and pipelines is rather limited at present. The chromates are used in dilute solution in this capacity, in concentrations ranging from 100 to 2,500 ppm (1/10,000 to 1/400), but this concentration is still above the threshold of sensitivity for some persons. Leaks about pumps and couplings may contaminate the whole work area with the chromate solution, and by evaporation more concentrated residues are formed. Dermatitis[9] and possibly chrome ulcers have been reported as complications from this use.

Zinc chromate primer, commonly called "prime," is used as a corrosion-inhibitive paint on most aluminum and magnesium airplane parts after anodizing. With employment in the aircraft industry at a high level once more, workers using this paint probably constitute the largest group currently exposed to chromates. Although the zinc chromate is found in dust in the plant and is sprayed in the form of paint on many of the airplane parts, there has been no report of a perforated septum or systemic reaction among workers in the industry. Dermatitis is frequently seen.[10]

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3. Meyers, J. B.: Acute Pulmonary Complications Following Inhalation of Chromic Acid Mist: Preliminary Observations of 2 Patients Who Inhaled Massive Amounts of Chromic Acid, Arch. Indust. Hyg. **2**: 742 (Dec.) 1950.

4. Pascale, L. R., and others: Chromium Intoxication: With Special Reference to Hepatic Injury, J. A. M. A. **149**: 1385 (Aug. 9) 1952.

5. Machle, W., and Gregorius, F.: Cancer of the Respiratory System in the United States Chromate-Producing Industry, Pub. Health Rep. **63**: 1114 (Aug. 27) 1948.

6. Edmundson, W. F.: Chrome Ulcers of the Skin and Nasal Septum and Their Relation to Patch Testing, J. Invest. Dermat. **17**: 17 (July) 1951.

7. Harris, M. C.: Contact Dermatitis Due to Contact with Chrome 17 Per Cent Steel Identification Tags of the United States Navy, J. Allergy **16**: 299 (Nov.) 1945.

8. Hall, A. F.: Occupational Contact Dermatitis Among Aircraft Workers, J. A. M. A. **125**: 179 (May 20) 1944.

9. Winston, J. R., and Walsh, E. N.: Chromate Dermatitis in Railroad Employees Working with Diesel Locomotives, J. A. M. A. **147**: 1133 (Nov. 17) 1951.

Chrome tanning as an improvement over vegetable tanning for certain kinds of leather achieved commercial significance about 1900. Trivalent chromic sulfate and in some processes hexavalent sodium dichromate are the materials used. Chrome sores and chromate dermatitis were found early to be an industrial hazard in this field. At present, their incidence has been reduced by protective measures and by the substitution of mechanical for manual handling of the hides where possible. Three-quarters or more of the leather in the United States is tanned by this process. These leathers contain 3.9 to 6.9% chromium as chromic oxide in hide substance, i. e., minus water and fat. Theoretically, when tanning is completed, all this chromium is in trivalent form in close chemical combination with the hide protein. Since apparently trivalent chromium is never sensitizing, the frequent coexistence of dermatitis from shoe leather and hypersensitivity to chromate is difficult to explain. There are several possible explanations: There may occasionally be small amounts of residual chromate that was not reduced during the "two bath" tanning process. Some of the trivalent chromium may be oxidized to chromate during some subsequent processing of the leather. Chromate may be used in the dyeing of some leathers. Finally, there may be some peculiar relationship between shoe leather dermatitis and positive reactions to chromate patch tests, such as has been found in cement eczema.[11] Further studies should be carried out to clarify these points.

Large amounts of chromate are used for wood preservation. The solutions contain chromated zinc chloride, and some exposure of the workers occurs. The wood is impregnated with the chemicals, which may be a hazard for those handling it. There has been no report of dermatitis in this industry or from this material.

In photoengraving, ammonium dichromate is used as a photo sensitizing agent [2] and often is handled rather carelessly. Here again a large part of the shop area may be contaminated to some extent with dried chromate. This material is used for the same purpose in lithography.[2] In blueprinting a bichromate bath is used for fixing the color in the paper. Finished blueprint paper has a small percentage of chromium compound in it and may cause dermatitis. One analysis of this paper showed 0.024% chromium, some of which is in hexavalent form. In all these trades, as in chrome plating, chrome dermatitis is well known, and most workers know of someone who has it or who has had to leave the trade because of it.

Sodium bichromate is used extensively as a mordant or fixative for the dyeing of woolen cloth and fur. A dermatitis from this use has been observed in wool mill workers.

Except for zinc chromate, mentioned previously, the pigments used in paints, inks, rubber, and ceramics, namely, lead and barium chromate and trivalent chromium oxide, are very insoluble and seldom if ever cause dermatitis. These substances may sometimes contain traces of a soluble hexavalent chromate that will cause difficulty in the evaluation of patch tests.

The chief fields in which chromium salts are used extensively have been mentioned. They are also used in the manufacture of dry cell batteries, matches, and explosives, in fur and leather dyeing, in bleaching of fats and oils, and as reagents in the chemical industry. The foregoing discussion is, however, sufficient to indicate that chromate materials are widely used and that physicians should always be alert to the possibility of their being the cause of an occupational dermatosis.

MEDICAL ASPECTS OF CONTACT WITH CHROMATES

The medical aspects of contact with chrome compounds were reported in the literature as early as 1827.[1] Acute toxic reactions rarely occur except from accidental ingestion or the inhalation of concentrated mists such as are formed in electroplating.[8] After ingestion, symptoms usually appear in a few minutes or a few hours and are abdominal pain, vomiting, and diarrhea.[12] Traces of albumin are found in the urine. Toxic changes in the kidneys and the liver have been described.[13] Most patients have recovered without sequelae.

Inhalation of concentrated mists causes pulmonary congestion, with fever, cough, and production of sputum.[8] Productive cough may persist for as long as one year. The occurrence of toxic hepatitis, with jaundice and severe liver damage, has recently been reported in one worker and evidence of mild hepatic dysfunction in three others in the same group who were exposed over long periods to mists from a plating tank.[4] Excretion of chromium in the urine could be demonstrated in these patients.

Inhalation of chromate-containing dust by workers in ore processing plants over long periods (15 years) seems to have a carcinogenic effect on the lung. Pulmonary carcinoma occurred 16 times more frequently in these workers than in comparable groups.[5] While the series was not large, the figures are apparently significant. Similar observations have not been reported from any other industry in which chromate is used.

CHROME ULCER AND PERFORATED SEPTUM

Other types of lesions that are of more interest to the dermatologist are the chrome ulcer and perforation of the nasal septum. Perforation of the nasal septum obviously can occur only in shops in which there are mists or dusts containing chromate. First, a painless ulcer appears on the lower cartilaginous portion of the nasal septum. In as short a time as one to two months a perforation may develop. These lesions usually cause little or no discomfort, and the patients seldom consult their physician about them. Edmundson found 61% of 285 workers in a primary chromium chemical manufacturing plant to have perforated septums.[6]

Chrome ulcers are well known in the tanning, electroplating, and chroium-chemical-producing industries. They form only when the chromate is introduced into a break in the epidermis. Thus while the hands and arms are the commonest sites, the ulcers may occur anywhere on the body. In the aforementioned chemical plant, 69.5% of the workers had chrome ulcers or scars of such ulcers.[6] The typical ulcer has definite characteristics. It is a punched out lesion, 2 to 5 mm. in diameter, with a raised collar-like indurated border several millimeters wide. It tends to take the shape of the preceding break in the skin. There is minimal inflammation, and the lesions are relatively painless, except when near a joint or subject to trauma. They usually heal, leaving a depressed atrophic scar, although hypertrophic scarring has been seen. No instance of malignant degeneration has been reported in a chrome ulcer or in a septal perforation. There apparently is no increased tendency on the part of workers in whom these lesions develop to become sensitized to chromates.[6] No reports were found in the literature on the amount of exposure or the concentration of chromate needed to produce an ulcer. The simple tests reported in the table give some information on these questions. All tests were made by the usual patch test technique, except that the materials were placed on scratches about 2 mm. long that were made with a knife point inserted just deep enough to draw blood. These observations suggest that very low concentrations of chromate may, under the proper conditions of time and contact, produce ulceration. The ulcers apparently are due to a toxic, necrotizing action of the chromate ion on living tissue, independent of its sensitizing properties. There was no allergic reaction or primary irritation with 0.5% dichromate on intact epithelium in the patient on whom the tests were done. At the higher dilutions, the acidity or alkalinity of the solution could not be responsible. It is interesting to note that solutions of the monochromate salts of sodium and potassium are alkaline in reaction but that the dichromate salts are acid, yet they act identically in the production of an ulcer or dermatitis.

CHROMATE DERMATITIS

The sensitization to chromate compounds that results in dermatitis is of great importance to industry and to dermatologists. It is difficult to judge from the literature how great the hazard is. It has been reported that as many as 25% of

10. (*a*) Hall.[8] (*b*) Ellis, F. A.: Occupational Dermatoses in Aircraft Workers: Chromate Dermatitis, Occup. Med. **2**: 452 (Nov) 1946.

11. Jaeger, H., and Pelloni, E.: Epicutaneous Tests to Bichromates, Positive in Cement Eczema, Dermatologica **100**: 207, 1950.

12. Goldman, M., and Karotkin, R. H.: Acute Potassium Bichromate Poisoning, Am. J. M. Sc. **189**: 400 (March) 1935.

13. Pascale,[4] Goldman and Karotkin.[12] Smith, A. R.: Chrome Poisoning with Manifestations of Sensitization: Report of a Case, J. A. M. A. **97**: 95 (July 11) 1931.

workers exposed to chromate in a lithographing plant had chromate dermatitis during the first year.[14] This incidence is certainly higher than that in any other group studied. Schwartz and Dunn found that 4% of workers who maintained an air conditioning installation in which chromate was used in the circulating fluid had positive reactions to 3% dichromate in patch tests; however, not all of the reactors had dermatitis. From the data in Hall's paper, "Occupational Contact Dermatitis Among Aircraft Workers,"[8] it would seem that in 5 to 6 workers out of every thousand a chromate dermatitis due to zinc chromate primer paint develops each year. Ellis, in a similar group, estimated the incidence at about one per thousand per year.[10b] Rough estimates of sensitivity made from data from another large aircraft factory that has about 12,000 workers in contact with the same material agree with Hall's findings. In a small group of diesel locomotive workers that I studied the rate was about 10 per thousand per year, or 1%.[9] It would seem from the above that the probable limits of incidence of dermatitis in any large group of persons exposed to hexavalent compounds will be between 1 and 10 per thousand per year. This will probably vary greatly with the type of exposure and the turnover of employees.

It would be well here to amplify and substantiate as far as possible the statement made several times in the paper that only the hexavalent chromate ion is a sensitizer and that metallic chromium or the trivalent compounds are not sensitizing substances. There were no reports in the literature examined suggesting that a hypersensitivity reaction to trivalent chromium occurs. The one report of reaction to metallic chromium [7] was not proved by proper patch testing and may well have been a reaction to nickel. Several dermatologists of wide experience in industrial dermatology and cutaneous allergy stated that they knew of no report or instance of reaction to trivalent chromium. Three patients were tested who had positive patch tests to very weak solutions of bichromate (1/10,000 and 1/20,000) showed no reactions to solutions of trivalent salts [11] nor to metallic chromium. Three-fourths of all shoes are made with chrome-tanned leather containing 3 to 6% trivalent chromium. The wearing of shoes made from this leather is, in effect, a mass patch test to trivalent chromium. No instance of sensitization has ever been reported. These facts give a substantial basis for the assumption that sensitization to trivalent chromium or metallic chromium does not occur.

There is little in the literature regarding the incidence of chromate sensitivity in the general population. In a group of eczema patients 12% were found to have positive patch tests for chromate. In a group of patients with other dermatoses 5% had positive reactions.[14] Among 60 patients in a tuberculosis sanitarium, I found three with a definite positive reaction to 1% postassium dichromate. This is about a 5% incidence of definite positive reactions. Only two, or 3½%, gave a definite reaction to 0.5% dichromate. In another group of 60 hospital patients tested with 0.25% dichromate there were no positive reactions. These groups are all too small to be statistically significant but it would appear that there is a higher incidence of positive patch tests to 0.5% or 1% dichromate in the general population than of dermatitis in industrial workers exposed to chromate. Perhaps 0.25% dichromate would be a better test dilution to demonstrate the more marked degrees of hypersensitivity.

Little is known of the factors influencing sensitization. The concentration of the material seems to play little part. It would seem likely that there would be a high incidence of sensitization among the workers in the chromium-chemical-producing plant who had the high incidence of ulcers and perforated septums and who obviously were often exposed to heavy concentrations of chromate. Edmundson found only 2 of 56 of these workers with ulcers or septal perforations who had a positive 24-hour patch test to 0.5% sodium dichromate.[6] These two gave a history of dermatitis but did not have it at the time of examination. This represents only 3.5% of the group, or about the same incidence that was found in the previously mentioned sanitarium patients who were tested with the same material. This is a higher incidence than was found in the other industrial groups, but again these groups are too small for an accurate evaluation. Some investigators in this field feel that dilute solutions are more likely to sensitize.

An interesting work was recently reported in Switzerland by Jaeger and Pelloni, who found that 30 of 32 patients, or 94%, with cement eczema had a positive patch test to 0.5% dichromate. Traces of chromium were demonstrated in several samples of cement that were tested. The type of chromium found was not mentioned, and no explanation of this peculiar clinical finding was advanced.[11]

Only general statements can be made about the effect of the duration of exposure on sensitization. Most men seem to agree that the great majority of exposed workers who will develop a sensitivity do so during the first nine months they work with chromate.[14] However, dermatitis may appear in one week or not until after as long as nine years of exposure. A most important point is that sensitization does not increase in proportion to the duration of exposure.

The reaction threshold of those sensitive to chromate may be very low. One patient with a shoe leather dermatitis reacted to a 1:20,000 solution of sodium dichromate. For routine patch testing, 0.5% dichromate is the recommended strength. Ellis felt that this strength might give questionable or negative reactions [10b] and suggested a 5% chromate solution. As mentioned above, 0.25% may give a more accurate test of hypersensitivty. When a high degree of sensitivity is suspected, a 0.05% solution should be used as a first test and even this may give a 3+ reaction. Delayed positive reactions that do not appear for 24 to 48 hours after the test period are sometimes seen and should be routinely watched for.

Results of Patch Tests with Various Concentrations of Chromium Compounds Applied to Superficial Skin Abrasions

Material	Length of Exposure	Reaction			
Chromic acid, 2%	24 hours	Crusted lesion 3 weeks			
Sodium dichromate, 0.5%	Reapplied daily 3 days	Crusted lesion 3 weeks			
		3 days	1 week	2 weeks	3 weeks
Potassium chromate, 0.5%	8 hours a day for 3 days	3*	2	1	1
Sodium dichromate, 0.05%	8 hours a day for 3 days	2	1	0	0
Sodium dichromate, 0.005%	8 hours a day for 3 days	1	1	0	0
Zinc chromate, pure	8 hours a day for 3 days	1	0	0	0
Lead chromate, pure (insoluble)	8 hours a day for 3 days	0	0	0	0
Chromic nitrate, 10% (trivalent)	Reapplied daily 3 days	±	0	0	0

* These numbers indicate roughly the size of the ulcer and the duration of a crusted lesion. Thus "3" represents a shallow crusted lesion 2 by 4 mm. in size, "2" a lesion 1.5 by 3 mm., and "1" a lesion 1 by 2 mm. The ± indicates redness in the area of the scratch but no ulceration.

The question of preemployment patch testing is a controversial one. Such tests would not demonstrate those who will become sensitive after several months of exposure. However, it seems that in such industries as the aircraft and railroad diesel shops preemployment patch testing might be of benefit in pointing out some potential dermatitis patients and would reveal a few who could not tolerate even minimal exposure. The danger of sensitization developing from a 48 hour patch test seems rather remote, judging from the usual history of the dermatitis appearing after several weeks or months of contact. Certainly information obtained from a large series of preemployment patch tests concerning the significance of negative, questionable, and positive reactions as compared to the working exposure to chromate compounds would be very worth while. Further, more careful observations on factors of time and intensity of exposure relative to sensitization would be valuable.

14. Engelhardt, W. E., and Mayer, R. L., cited by Pirilä, V., and Kilpiö, O.: On Dermatoses Cased by Bichromates, Acta dermat-venereol. **29**: 550, 1949.

CLINICAL CHARACTERISTICS

Morphologically chromate dermatitis varies from an acute vesicular weeping eruption, to dry, erythematous, slightly elevated squamous plaques that may be rather well circumscribed with normal skin between. Sometimes grouped papular lesions are seen. The commonest sites are the dorsum of the hands, wrists, and forearms. The neck and eyelids may be affected or any other part with which the chromate comes in contact. While there are no specific morphological characteristics, in a plant where these eruptions are frequently seen they are soon spotted as an entity.

Acute or minimal eruptions may heal in two to three weeks. The dry patchy eczematous eruptions may be very slow to heal, lasting sometimes six weeks to six months even after the patient is removed from all contact with the material. This is particularly true if the eruption is of several months' duration or if it is a second or third exposure. Chromate dermatitis often differs from the usual contact dermatitis in its patchy distribution and longer course.

TREATMENT AND PROPHYLAXIS OF CHROMATE DERMATITIS

Early detection of chromate dermatitis is of utmost importance if prolonged disability is to be avoided. There is apparently no "hardening" or increased tolerance of workers on further exposure to chromate, at least not after a sensitivity dermatitis has developed. On the contrary, with subsequent exposure each attack seems to be severer and more extended. As mentioned above, however, the likelihood of sensitization does not seem to increase with the duration or intensity of exposure.

Treatment should consist of wet dressings when indicated and bland local applications. In stubborn cases x-ray treatment will probably hasten healing. Dimercaprol (BAL) in a 3% ointment has been advocated for chromate dermatitis, although the evidence of its effectiveness is not very striking.[15] Injections of dimercaprol seemed to have little effect on the eruption of one patient on whom it was used.[9]

The problem of prevention or control of chromate dermatitis is of utmost importance. Where dust, mists or sprays are encountered, proper ventilation, plant cleanliness, exhaust fans, and ducts, protective clothing, and masks are indicated. Where chromate powder and solutions are used, these measures and particularly careful handling to prevent contamination of the work area are important.

Workers handling chromate should be provided with proper protective clothing such as rubber gloves and aprons when it is feasible. Facilities for immediate cleansing should be provided for workers who must come in contact with concentrated chrome compounds. Contaminated areas should be thoroughly washed down and cleansed before men work in them. Equipment should be designed to facilitate the handling and to prevent or minimize the leakage of the solutions.

The workers should be told something of the potentially harmful nature of the substance with which they are working, and the extent of the danger, which actually is not great, should be explained. Otherwise exaggerated stories of the hazard soon spread through the plant and the whole industry, for example, the stories of the so-called prime poison in the aircraft industry and diesel itch in the railroad industry. Workers should be impressed with the importance of reporting for examination at the first appearance of an eruption. It can then be determined by patch testing whether or not chromate is the offending substance. If the sensitivity is not severe, the worker may attempt to resume work with extra precautionary measures. If the dermatitis then recurs, he should immediately be removed from contact with the material.

Chrome compounds present a relatively small industrial hazard even in the industries where they are used. If the danger is recognized and suitable precautionary measures are taken, they can be safely used wherever such use is indicated.

SUMMARY

Chromium in metallic form and in its trivalent and hexavalent forms is important in many manufacturing and industrial processes. Some of these are electroplating, anodizing and other anticorrosive metal treatments, tanning of leather, pigments and anticorrosive paints, mordanting of wool, fur, and leather, and photoengraving and lithography.

Workers come in contact with chromates in the form of mist or dust that is inhaled and in solution or solid form. Inhalation may produce acute pulmonary symptoms or chronic hepatic intoxication; in some rare instances of long exposure to dust, carcinoma of the lung is apparently produced. Perforation of the lower nasal septum may result from inhalation of mists or dust. Chrome ulcer is produced by contact of the material with an abrasion or any break in the epidermis.

Dermatitis due to contact of chromate-sensitive persons with these substances is the most important of the industrial hazards encountered. Apparently only the hexavalent compounds are sensitizing. The incidence of such sensitivity and the factors influencing its production are discussed.

Chromate dermatitis is often patchy in distribution and more prolonged in its course than the usual contact dermatitis. Prophylactic measures include protective clothing, proper designing of machinery, and industrial engineering to reduce or to prevent contact with the material and contamination of work areas. Education of the workers as to the nature of the danger and the early detection, investigation, and management of any eruption that occurs are of great importance.

1810 Medical Arts Bldg. (2).

15. Cole, H. N., Jr.: Use of Dimercaprol (BAL) Ointment in Chronic Chrome Dermatitis, A. M. A. Arch. Dermat. & Syph. **67**: 30 (Jan.) 1953.

MEDICAL MOTION PICTURES

NEW FILM ADDED TO A. M. A. MOTION PICTURE LIBRARY

Principles of Fracture Reduction: 16 mm., color, sound, showing time 30 minutes. Produced in 1953 by Churchill-Wexler Productions, Los Angeles, for the Veterans Administration. Procurable on loan (service charge $3.00) from Committee on Medical Motion Pictures, American Medical Association, 535 North Dearborn Street, Chicago 10.

This film presents first, the cardinal principles for closed reduction of fractures employing well-executed animated drawings. Then, using both patients and models, it illustrates the application of these principles as they apply to the splinting of fractures both in first aid and in treatment. The use of splints, traction, and plaster of Paris is well illustrated, as well as the manipulation of several simulated fractures using local anesthesia and various methods of improvised traction to facilitate the manipulative reduction. Some of the manipulations using improvised traction are shown by model in a farm house situation where it was impossible to obtain preliminary roentgenograms. Although this may at times be necessary, wherever possible, manipulation and reduction should be deferred until roentgenologic study is possible. In a teaching film it seems unfortunate that this point is not stressed. The photography, animation, and narration are of high quality. In the last section the use of the model seen previously makes the film slightly less realistic and less interesting than it might have been, but this is not a serious fault. On the whole, the film is excellent and should prove of value to both medical students and practicing physicians. It probably represents the best elementary film now available on this subject.

Fred Bauer Waits: 16 mm., black and white, sound, showing time 28 minutes. Produced in 1952 by Victor Weingarten, New York, for, and procurable on loan or purchase ($45.00) from, Health Information Foundation, 420 Lexington Ave., New York 17.

The primary purpose of this film is to convince nonmedical persons that early diagnosis and treatment of vague illness prevents considerable worry, emotional dislocation of family, feeling of insecurity in children, and prolonged treatment when diagnosis is ultimately made. The father of the family suffers a complex of symptoms that he mistakenly thinks is

cancer and, because of that attempt at self-diagnosis, delays treatment until his diabetes is far enough advanced to be very troublesome to him, and very disturbing to his family. His preoccupation with the idea that he has cancer is ultimately picked up by the family, causing even the children to exhibit the insecurity associated with the possible loss of a parent. When his diabetes is discovered and when he is under adequate treatment, the family troubles disappear and normal family relationships are resumed.

The developing symptoms of diabetes are quite obvious, but, through the confusion of some of these symptoms with the keys to cancer detection, the father is led to a false diagnosis of his condition. This situation dramatically points out the dangers inherent in self diagnosis by a nonmedical person. This film would be most suitable for adult groups. With proper presentation by a well-prepared instructor, it could be used in the 11th and 12th grades. The photographic quality of this motion picture is excellent. The sound quality, however, is below average.

BUREAU OF LEGAL MEDICINE AND LEGISLATION

MEDICOLEGAL ABSTRACTS

Practice of Healing Art Not Interstate Commerce.—This was an action for damages for an alleged violation of the Sherman Anti-Trust Act. From a judgment in favor of the defendants, the plaintiff appealed to the United States court of appeals, tenth circuit.

The plaintiff, a chiropractic institution, filed a suit for damages against the medical society of the city and county of Denver; a number of present and former members of the state board of health; a number of former and present officials of the medical society; and a number of individuals, alleging, among other things, that the defendants combined and conspired to prevent the licensing of the plaintiff institution by the proper authorities of the state of Colorado to prevent the operation and maintenance of such institution and to allocate to the members of the medical profession within the state of Colorado the entire practice of the healing arts within that state, to the exclusion and restraint of the practice of chiropractic. The defendants moved to dismiss the action on the ground that it did not state a claim on which relief could be granted, and the motion was sustained, hence this appeal.

The practice of the healing arts in Colorado, including chiropractic, is wholly local in character, said the court of appeals. The alleged conspiracy and the acts alleged to have been done in furtherance thereof had for their purpose and object the monopolization and restraint of purely local activities. No price fixing or price maintenance for professional or other services was involved. There was no intent to injure, obstruct, or restrain interstate or foreign commerce. The mere fact that a fortuitous and incidental effect of such conspiracy and acts may be to reduce the number of persons who will come from other states and countries to the Spears Hospital for chiropractic treatments does not create such a relation between interstate and foreign commerce and such local activities as to make them a part of such commerce. To come within the purview of the Sherman Act, the restraint of commerce or the obstruction of commerce must be direct and substantial and not merely incidental or remote. The conspiracy or combination must be aimed or directed at the kind of restraint that the Act prohibits, or such restraint must be the natural and probable consequence of the conspiracy. Where, however, the object and purpose is to restrain or monopolize activities or matters purely local in character, those facts may be considered in determining whether the effect on interstate or foreign commerce is direct and substantial or only incidental, indirect, and remote. Here, the court said, the purpose and object of the conspiracy and of the means adopted to effectuate it were to restrain the practice of chiropractic and to allocate to the medical profession the practice of the healing arts in Colorado. It is this exclusively local aim and not the fortuitous and incidental effect upon interstate and foreign commerce that gives character to the conspiracy. The effect upon interstate and foreign commerce was fortuitous and remote and not direct and substantial. We conclude, therefore, said the court, that in the instant case there was no direct, immediate, or substantial effect on interstate or foreign commerce bringing the alleged conspiracy within the scope of the Sherman Act.

The court of appeals specifically stated, however, that it was unnecessary to pass upon the question of whether the practice of the healing arts, including chiropractic, is trade or commerce within the meaning of the Sherman Anti-Trust Act. Accordingly the judgment of the trial court sustaining the defendants' motion for dismissal was affirmed. *Spears Free Clinic and Hospital v. Cleere, et al., 197 F. (2d) 125 (1952).*

BUSINESS PRACTICE

The following material is based on a public relations manual issued by the Public Relations Department of the American Medical Association.—ED.

ADJUSTMENT OF FEES

No person needs to go without medical care in this country because he is unable to pay for it. Every day, physicians provide care for persons who, for good reasons, are financially unable to meet their medical bills. If people complain that medical care is unavailable to those without funds, it is becaues they are unaware that each year physicians quietly and modestly give millions of dollars worth of free medical care. Many medical societies have made public their willingness to provide medical care to anyone who cannot pay for it. These programs are meeting with good public relations effects, but the task of deciding whether to reduce a fee or cancel it entirely in a hardship case falls to the doctor.

There are two prevailing philosophies on this question. One belief is that a doctor should reduce his fee but not cancel it, in order to save the patient's pride. The man who pays a small sum toward his expenses does not feel like a charity patient. The second philosophy is that a doctor should never reduce but completely cancel a fee if necessary. This evolves from the thought that a doctor should not bargain with his patients about charges. The inherent dangers in too readily reducing or canceling medical fees are that it encourages the irresponsible persons who believe the world owes them a living and it smooths the way for the cheats who dress up in shabby clothes when they come to the doctor to give the impression they are unable to pay for their medical care. Although the poverty of a patient should command the gratuitous services of a physician, it is difficult for a physician practicing in a large city to know whether a patient can pay for care. Patients must be educated to discuss their financial problems with their doctor before contracting for care.

Here are some suggestions to guide a physician in deciding whether a fee should be reduced or canceled. First, he should try to get adequate information about the patient's financial status. It is important to encourage advance fee discussions. Secondly, when a patient requests a lowered fee, he should investigate locally to learn whether the person is truly needy. If it is possible to determine if a needy patient is eligible under local and state public assistance programs, the physician can put him in contact with these groups. Thirdly, when referring patients to another physician, it is helpful to send financial information. And, finally, he should make financial arrangements that best serve the interests of the patient.

Sometimes the generosity of a physician backfires. It is dangerous to reduce a fee for an operation that the patient did not survive. This implies negligence or incompetence on the part of the physician and could form the basis for a malpractice suit. In such cases, it is better to submit a bill for the amount originally agreed on. Most patients are anxious to pay their own way. The physician often can settle the fee problem by following the directives of his heart.

THE LEISURE CORNER

MODEL RAILROADING: A FATHER-AND-SON HOBBY

As the Yuletide season approaches, many readers of the "Leisure Corner" will, as the result of ardent petitions advanced by a wide-eyed, mechanically-minded younger generation, undoubtedly find that model railroading also has an equally strong fascination for them. Interest in model scale railroading as a popular father-and-son hobby is a phenomenon based partly on a mutually shared interest that first takes root in early childhood and that later expands during adulthood. Dyed-in-the-wool participants are convinced that the hobby affords an assortment of challenges to the combined aptitudes and ingenuities of the two generations. Actually, the creation of a model railroad is an expression of ability to create, plan, and perform, and this is soon made evident in the need for painting, assembling, carving, bending, soldering, molding, drilling, and sawing. No two model railroads are similar, and that is one of the reasons why model scale railroading is a hobby with such widespread appeal to young and old alike.

The imagination of father-and-son model railroaders will channel their energies into any one of dozens of intriguing construction situations—from the building of a simple railroad to a complicated system with elaborate signals; junctions with three tracks branching out of four; lighting arrangements that produce effects of daylight and nighttime or thunderstorms and sunsets; and create brightly colored passenger trains and lengthy freight trains, which traverse make-believe countrysides interspersed with towns, valleys, and mountain ranges. Perhaps wistful memories of a childhood spent in a peaceful pre-World War I era will influence the physician-father in his decision, and, in that case, circus trains with special equipment and gay colors will fascinate the two generations of model train magnates. Again, a model railroad need not necessarily represent the latest form of twentieth century transportation; for some hobbyists, broad-stacked, brightly ornamented eight-wheeled engines with polished brass trimmings and huge headlights hold definite appeal. On the other hand, if the senior-and-junior railroaders are enchanted by rural life or teeming industrial environs, small towns, fishing villages, mountain resorts, freight yards, oil wells, quarries, or even steel mills these, too, can be incorporated in a model railroad system. The point is that model railroading permits the imagination to run riot, enabling father and son to pursue their own individual bents and, at the same time, serving up heaping doses of that contented feeling.

Model railroading provides its devotees with sugar-coated training in a half-dozen useful crafts. As most hobbyists quickly learn, newcomers will often find themselves unfamiliar with the numerous techniques characteristic of this mechanical hobby. However, they soon become proficient in drilling and tapping holes and in working with sheet metal and fragile wood; they soon learn a little about soldering and about how dies and patterns are made; something about electrical intricacies and how to differentiate a weak joint from a well-engineered joint; and how to distinguish between a well-made mechanism and a shoddy mechanism. Hobbyists will frequently be surprised to discover a newly acquired dexterity in the use of their hands, so that tasks once regarded as being impossible to perform turn out to be simple, routine matters. This, of course, is not to imply that an apprenticeship in model railroading will convert physicians and their offspring into qualified mechanical engineers; but the abilities that are acquired while in pursuit of the hobby will make its participants more useful persons to have around the house or home. At least, the wife and mother of the household may eventually find this to be the case.

Nearly all model railroads grow piecemeal, usually starting with the assembly of a rolling stock from a kit and later adding several cars and a locomotive, as the track plan takes shape in the minds of the builders. Gradually, more and more models are accumulated, first for an entire train, then for two trains. When this stage is reached, the hobby begins to multiply in its manifold possibilities, for a minimum of two trains enable hobbyists to operate train service on a model railroad in a realistic manner. And as the model railroading venture grows, there is always the strong possibility that other members of the family—and this includes mother and the younger sisters—will interest themselves in the hobby. It has been claimed that few hobbies succeed in bringing teen-agers back into the family group as effectively as model railroading; and, indeed, the most desirable scenic effects have often been created by enthusiastic mothers of the household.

In order to eliminate stooping on the part of the older hobbyists, almost all scale model railroads are now constructed away from the floor. Wood is used for the supporting frames, and track is usually laid on flat strips of wood so that it can be unscrewed at will when changes are contemplated. Scenic terrain is composed of plaster or some other moldable material spread over a lath of wire screen or cloth; buildings generally consist of wood or cardboard; locomotives are constructed of metal; and cars are made either of metal, wood, or plastic. The trend among model railroad hobbyists is to build cars and engines from kits that contain every construction part required. Recent growth of interest in scale model railroads is partly indebted to the toy train field. Scale modelers speak of toy trains as "tinplate," many model rail systems being derived from a Lionel, American Flyer, or Marx Christmas train set. In reality, scale model railroading is not as suitable a hobby for very young boys as is the tinplate train, but as the youngsters become teen-agers, the skills and crafts associated with scale model railroading provide a distinct advantage.

The principal difference between finished tinplate and scale equipment lies in the track. Tinplate track is constructed in sections that can easily be taken apart; on the other hand, in scale track the proportions are more accurate, the curves are broader, and the track can be made to serve in a more permanent form. Tinplate passenger trains are built to be undersized and short, so that they can readily traverse the sharp curves inherent in sectional track. Tinplate trains employ a sequence reverse, and the motors operate on alternating current derived from a transformer. Scale trains utilize an improved reverse scheme that depends on direct current coming from a power pack. A transformer cannot be used unless a rectifier is employed to convert it into a power pack. Scale model railroads usually have two running rails for electric power distribution. When a third rail is desired, scale model railroaders locate it to either side of the track. Although track is very easy to lay, the beginner can be fooled. It is therefore a good idea to first build a small test yard before commencing construction of a more permanent type of railroad system. In model railroading it is important to have every part of the model railroad truly proportional to every other part. Passenger cars on a real railroad are generally twice as long as box cars, as they are in properly proportioned scale railroads.

Today there are four scales for which a variety of equipment is available. Model railroaders usually identify them by letter for each gauge of track—O, S, HO, and TT. Gauge is defined as the distance between inside rail faces of the track; standard gauge is 4 ft. 8½ in., and, in modeling standard gauge equipment, the scale should properly relate the track and cars. Scale is the ratio of size the models bear to the original and is usually stated in terms of fractions of inches or millimeters in the model to 1 foot in the original. Gauge O has proved to be the favorite type of gauge for many hobbyists who want detail in cars and locomotives. HO gauge is about half the size of O gauge, and OO is a little more than half the size of HO. O gauge cars cost approximately twice as much as HO equipment; engines range anywhere from 25% to 75% more in price. If there is any uncertainty about which gauge is best to buy, it might be well to experiment with a car kit and a limited amount of track material in each gauge. When the cars and track are assembled, it is soon possible to obtain a clear notion about construction preferences. Once this is determined, model scale railroading is well on its way to becoming an enjoyable, lifelong hobby.

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MEDICAL LITERATURE ABSTRACTS

UNITED STATES

A.M.A. Arch. Ind. Hyg. & Occupat. Med. Chicago

8:205-298 (Sept.) 1953

Chronic Bronchopulmonary Disease Due to Inhalation of Sulfuric Acid Fumes. A. Goldman and W. T. Hill.—p. 205.
Current Lines of Attack on Smoke Problem in Britain. P. C. G. Isaac. —p. 212.
Chronic Oral Toxicity of Di (2-Ethylhexyl) Phthalate for Rats, Guinea Pigs, and Dogs. C. P. Carpenter, C. S. Weil and H. F. Smyth Jr. —p. 219.
Tetrachlorethylene Exposure in Small Industry. H. R. Coler and H. R. Rossmiller.—p. 227.
Dust Counting by Most Probable Number Method. H. M. Chapman. —p. 234.
Motivating Employees for Industrial Health. H. K. Abrams.—p. 246.
Physical Basis of Hearing Damage and Tentative Damage Risk Criterion for Steady-State Noise. H. C. Hardy.—p. 250.
Effect of Diet on Susceptibility of Rat to Poisoning by 2,4-Dinitrotoluene. M. E. Shils and L. J. Goldwater.—p. 262
Toxicity of 2-Ethylhexyl Diphenyl Phosphate: II. Metabolic Fate in Man and Animals. J. F. Treon, J. Cappel and H. Sigmon.—p. 268.
Id.: III. Studies of Extraction of Santicizer 141 from Polyvinyl Chloride Films by Foodstuffs Under Various Conditions of Storage. J. C. Kaskie.—p. 281.
Id.: IV. Skin Sensitization Studies of Santicizer 141. L. K. Halpern and R. S. Weiss.—p. 284.
Small Chamber for Studying Test Atmospheres. C. J. Spiegl, L. J. Leach, K. E. Lauterbach and others.—p. 286.
Chronic Oral Toxicity of Ethyl Phthalyl Ethyl Glycolate in Rats and Dogs. H. C. Hodge, E. A. Maynard, H. J. Blanchet Jr. and others. —p. 289.

Alabama State Medical Assn. Journal, Montgomery

23:59-90 (Sept.) 1953

*Intravenous Anesthesia for Obstetrical Delivery. E. Rucker.—p. 59.
Outpatient Treatment of Hypertension with Hexamethonium and Apresoline. W. P. Galen and L. L. Johnson.—p. 64.
*Pheochromocytoma: Report of Case in Nine Year Old Negro Male. P. M. Goldfarb.—p. 70.
Hypersensitivity to Gamma Globulin: Case Report. W. J. B. Owings. —p. 74.

Intravenous Anesthesia for Obstetrical Delivery.—Thiopental (Pentothal) sodium intravenously, combined with procaine infiltration of the abdominal wall, was used as method of anesthesia in 90 cases of cesarean section. There were no maternal deaths. The effect on the infant was minimal. Most of the babies breathed as soon as the nose and mouth were cleared by suction. Oxygen under pressure was used in a few cases in which there was some depression of the baby's respiration. The same type of anesthesia was employed in 179 women for ligation of the fallopian tubes in the puerperium as a method of sterilization. Thiopental sodium was used as the anesthetic agent for 473 patients who underwent minor procedures, such as curettage of the uterus, incision and drainage of abscess of Bartholin's gland, removal of secundines, and biopsy and cauterization of the cervix. Thiopental sodium is satisfactory for short procedures. In combination with procaine infiltration of the abdominal wall, thiopental is an effective anesthetic for cesarean section and puerperal sterilization. Pentobarbital (Nembutal) sodium in combination with meperidine (Demerol) hydrochloride and scopolamine (Hyoscine) was used for vaginal delivery in 6,257 patients; 100 mg. of meperidine and 0.6 mg. of scopolamine intramuscularly in combination with 200 mg. of pentobarbital sodium orally were given as soon as the patient's labor became uncomfortable, with little regard to cervical dilatation. Pentobarbital sodium was given intravenously when the previous procedure was no longer sufficient to make the patient comfortable. Pentobarbital sodium was supplemented by scopolamine in 0.3 mg. doses intramuscularly each two to three hours as indicated, and by a second or third intravenous injection of pentobarbital sodium varying from 200 to 350 mg., depending on the patient's response. Additional anesthesia was generally needed when the cervix was fully dilated. This was obtained by additional pentobarbital sodium intravenously, or by additional meperidine hydrochloride intravenously in doses of 100 mg. The author was more inclined to use meperidine hydrochloride than additional pentobarbital sodium for delivery, if the total dose of pentobarbital sodium was near 1,000 mg. Pentobarbital sodium intravenously combined with scopolamine, meperidine hydrochloride, and pudendal nerve block proved to be an effective way of controlling pain for vaginal delivery. The use of pentobarbital sodium seems to be contraindicated in patients in whom there is any impaired function of the liver. There is no one intravenous anesthetic agent that is entirely satisfactory in obstetrics; but by combining several drugs and varying the dosage it is possible to obtain satisfactory analgesia and anesthesia for the first and second stages of labor without unduly affecting the baby.

Pheochromocytoma.—A case of bilateral, malignant pheochromocytoma with hypertension is described in a 9-year-old Negro boy. Severe constipation was the outstanding symptom. It was so severe that it was impossible to perform any of the tests for detection of a pheochromocytoma. The constipation ultimately produced all the signs and symptoms of intestinal obstruction. Enemas gave poor results but produced an outpouring of epinephrine which increased the constipation as well as the strain on the heart and this eventually led to congestive heart failure. Weakness and sweating were prominent symptoms. The presenting symptoms were varied in 14 other cases of pheochromocytoma in children collected from the literature. Excessive sweating was prominent in nine patients. Severe constipation was not described in any of the 14 patients, and paroxysmal hypertension was described in only one. Pheochromocytoma should be considered in the differential diagnosis in all cases of hypertension in both children and adults.

American Journal of Medicine, New York

15:281-438 (Sept.) 1953

Metabolic Studies on the Human Heart in Vivo: I. Studies on Carbohydrate Metabolism of the Human Heart. R. J. Bing, A. Siegel, A. Vitale, F. Balboni, E. Sparks, M. Taeschler, M. Klapper and S. Edwards.—p. 284.
Postural Effects in Tetralogy of Fallot. P. R. Lurie.—p. 297.
Venous Blood Flow During Valsalva Experiment Including Some Clinical Applications. S. Candel and D. E. Ehrlich.—p. 307.
Decreased Hallucal Circulation, Early Manifestation of Vascular Disease in Diabetes Mellitus. M. Mendlowitz, E. B. Grossman and S. Alpert. —p. 316.
Mechanism of Accelerated Peripheral Vascular Sclerosis in Diabetes Mellitus. R. S. Megibow, S. J. Megibow, H. Pollaxk, J. J. Bookman and K. Osserman.—p. 322.
*Nor-epinephrine; Effect in Normal Subjects; Use in Treatment of Shock Unresponsive to Other Measures. J. H. Moyer, J. M. Skelton and L. C. Mills.—p. 330.
*Non-specificity of the Electrocardiogram Associated with Coronary Artery Disease. H. D. Levine.—p. 344.
Bronchomotor Tone: Neglected Factor in Regulation of Pulmonary Circulation. S. Rodbard.—p. 356.
Clinical Problems in Neuromuscular Physiology. D. Denny-Brown. —p. 368.

Arterenol Treatment of Shock.—In cases of shock, blood pressure must be raised before vital organs are damaged by lack of adequate perfusion; administration of fluids is often not adequate to this, and thus cases of "irreversible shock" arise.

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Titles marked with an asterisk (*) are abstracted.

Arterenol is a drug closely related to epinephrine, differing only in the absence of the N-methyl group but having different pharmacological properties in that it is primarily a peripheral vasoconstrictor and has only a minimal stimulant effect on the heart. It is of value in the treatment of shock because (1) it raises blood pressure rapidly, regardless of the cause of hypotension, (2) its effects are easily controlled for obtaining any desired blood pressure response, (3) it is a short-acting agent, and thus avoids the danger of excessive elevation of blood pressure, and (4) its side-effects are minimal. The authors observed the action of the drug in 25 normotensive patients, and in 44 patients in shock, including 14 with myocardial infarction, 9 with overwhelming infection, 6 with excessive hypotension secondary to medication, and 15 in surgical shock. All of the last group had previously failed to respond to adequate fluid replacement and blood transfusions. Results were encouraging: in only two patients of the 44 did the blood pressure fail to rise to normal with arterenol, and 24 patients recovered completely. It was not always possible to reverse postoperative "irreversible shock." The drug proved most useful in severe hypotensive states following the administration of certain drugs to excessively sensitive persons.

Nonspecificity of Electrocardiogram in Coronary Disease.—The shortcomings of electrocardiography are pointed out with a view toward emphasizing caution in interpreting findings and the importance of checking these against clinical evidence. Changes in the T-wave, in the RS-T segment, and in the QRS complex of the electrocardiogram generally reflect, respectively, myocardial ischemia, current of injury, or death of muscle. The T-wave, the most labile and least specific feature of the electrocardiogram, may be affected by a large variety of factors, only one of which is ischemia. Changes in the RS-T segment usually but not always correspond to acute muscle damage. It is generally transitory and rarely permanent. Like the T-wave this may indicate an anatomical or biochemical lesion. QRS changes practically always signify death or replacement of the heart muscle; this is generally associated with coronary artery disease. Rarely it may result from heart muscle damage from other causes. The electrocardiogram is quite accurate in the detection of acute myocardial infarction but inaccurate in the diagnosis of old or of multiple infarcts. It remains to be seen whether the newer vectorcardiography will attain a greater accuracy.

American Surgeon, Atlanta, Ga.

19:803-914 (Sept.) 1953

*Surgical Significance of Tumors in Identical Twins: A Short Review of the Literature and Report of Sympathicoblastoma Occurring in Monozygotic Twins. C. M. Lee Jr.—p. 803.
Respiration and Anesthesia. D. F. Proctor.—p. 812.
Surgery of Pulmonary Tuberculosis. J. H. Forsee.—p. 821.
Surgical Management of Adrenocortical Tumors: With Report of a Case. J. D. Hardy, F. H. Alley, R. S. Jones and E. P. Bowerman.—p. 833.
*Certain Practical Considerations in Management of Carcinoma of Lung: Based on an Analysis of 235 Fatalities. F. F. Boyce.—p. 846.
Appendicitis, Antibiotics, and Surgical Drainage. E. F. Fowler and J. A. Bollinger.—p. 858.
Further Experiences with Experimental Reconstruction of Common Bile Duct: Use of Autogenous and Homologous, Fresh and Preserved Grafts of Blood Vessel, Ureter and Common Duct. A. W. Ulin, L. Van Ess, J. Entine, A. E. Pearce and W. L. Martin.—p. 867.
Acute Appendicitis in Children. D. B. Corcoran.—p. 874.
Obstructive Enterostomy and Treatment of Obstruction of Small Bowel. H. A. Gamble.—p. 880.
Indications and Contraindications for Tonsillectomy. J. A. Harrill.—p. 889.
Subdeltoid Bursitis. J. H. Boland.—p. 892.
Laboratory and Clinical Evaluation of Antrenyl, a New Anticholinergic Drug, and Its Application to Surgery. M. P. Rogers and W. Barrett—p. 896.

Surgical Significance of Tumors in Identical Twins.—This report of sympathicoblastoma in monozygous twins is believed to be the first. A review of the literature shows that tumors that have been common to both monozygous twins are chondrous exostoses, medulloblastoma, glioma, adenofibroma and carcinoma of the breast, melanoma and retinoblastoma of the eye, congenital cystic tumors of the kidney, papilloma of the larynx, carcinoma and cystoma of the ovary, nevi of the skin, testicular sarcoma, and myoma and adenocarcinoma of the uterus. Of identical twin boys born July 29, 1951, twin B underwent surgical removal of a sympathicoblastoma in the region of the left kidney on Dec. 12, 1951. Laparotomy was advised for his brother, but refused by the mother. Roentgenotherapy did not improve the disease in twin B whose condition deteriorated rapidly until his death on March 10, 1952. Meanwhile, twin A, in whom a metastatic lesion had developed in the right temporal region, underwent an exploratory laparotomy on Jan. 24, 1952. A biopsy from the right temporal mass was taken at the same time. The liver was found to be infiltrated by metastases in both the right and left lobes. The primary tumor was in the right adrenal with extension into the kidney and the roots of the mesenteries. Twin A was not treated with roentgenotherapy, but with triethylene melamine, 1 mg. daily for three days. Later, at the age of 15 months, an apparently spontaneous remission occurred, but there remained several metastatic lesions, some of which were similar to those found in his brother at autopsy. The recognition of a tumor in one of a pair of identical twins should make the clinician alert to the possibility of a tumor in the other twin. In general, when the tumor is discovered in one twin during infancy or early childhood, the likelihood of concurrence is probably even greater than it is in adults, since the genetic factors are more likely to predominate. Although vigilance with respect to the apparently healthy twin is to be recommended at any age, it is especially important in the tumors of early life.

Management of Carcinoma of Lung.—Although surgical techniques have been greatly improved, the present yearly salvage of cases of carcinoma of the lung is barely 5%; this is due to the inadequacy of present diagnostic methods. Two-thirds to three-fourths of all patients are inoperable when first seen. There has been a steady increase in the incidence of this disease within the last 17 years, and it is on its way to becoming the most frequent type of malignant lesion in men. It is suggested that physicians should keep a close watch on men over 40 who complain of respiratory symptoms and that they refrain from relieving such symptoms without first finding out what is wrong with their patients, since a major cause of the high mortality rate of carcinoma of the lung is the relief of its symptoms by sulfonamides and, particularly, antibiotics. Cardiac, psychosomatic, and other diseases are frequently accepted as causes of respiratory symptoms that are really caused by carcinoma of the lung, or, if no diagnosis can be made, the patient is subjected to observation when actually an exploratory thoracotomy should be performed. Of the 235 patients to whom carcinoma of the lung proved fatal at the Charity Hospital of New Orleans between 1947 and 1952, 76 had typical histories, 98 more or less suggestive ones, 53 entirely atypical ones, and the remaining 8 died too soon for any information to be obtained. Diagnostic methods in carcinoma of the lung can be improved, particularly by a more careful study of roentgenograms taken fortuitously or for other reasons. We rely chiefly, at the present time in the diagnosis of the early, resectable case, on the prompt and bold resort to exploratory thoracotomy, on justifiable evidence if it exists or on simple clinical suspicion if it does not. Both internists and surgeons must display a greater boldness than they have in the past if lives are to be saved in carcinoma of the lung.

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Arterenol is a drug closely related to epinephrine, differing only in the absence of the N-methyl group but having different pharmacological properties in that it is primarily a peripheral vasoconstrictor and has only a minimal stimulant effect on the heart. It is of value in the treatment of shock because (1) it raises blood pressure rapidly, regardless of the cause of hypotension, (2) its effects are easily controlled for obtaining any desired blood pressure response, (3) it is a short-acting agent, and thus avoids the danger of excessive elevation of blood pressure, and (4) its side-effects are minimal. The authors observed the action of the drug in 25 normotensive patients, and in 44 patients in shock, including 14 with myocardial infarction, 9 with overwhelming infection, 6 with excessive hypotension secondary to medication, and 15 in surgical shock. All of the last group had previously failed to respond to adequate fluid replacement and blood transfusions. Results were encouraging: in only two patients of the 44 did the blood pressure fail to rise to normal with arterenol, and 24 patients recovered completely. It was not always possible to reverse postoperative "irreversible shock." The drug proved most useful in severe hypotensive states following the administration of certain drugs to excessively sensitive persons.

Nonspecificity of Electrocardiogram in Coronary Disease.—The shortcomings of electrocardiography are pointed out with a view toward emphasizing caution in interpreting findings and the importance of checking these against clinical evidence. Changes in the T-wave, in the RS-T segment, and in the QRS complex of the electrocardiogram generally reflect, respectively, myocardial ischemia, current of injury, or death of muscle. The T-wave, the most labile and least specific feature of the electrocardiogram, may be affected by a large variety of factors, only one of which is ischemia. Changes in the RS-T segment usually but not always correspond to acute muscle damage. It is generally transitory and rarely permanent. Like the T-wave this may indicate an anatomical or biochemical lesion. QRS changes practically always signify death or replacement of the heart muscle; this is generally associated with coronary artery disease. Rarely it may result from heart muscle damage from other causes. The electrocardiogram is quite accurate in the detection of acute myocardial infarction but inaccurate in the diagnosis of old or of multiple infarcts. It remains to be seen whether the newer vectorcardiography will attain a greater accuracy.

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Thyroiditis and Its Treatment. G. Crile Jr.—p. 67.
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Journal of Bone and Joint Surgery, Boston

35-A:539-804 (July) 1953. **Partial Index**

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*Use of Hyaluronidase in Orthopaedic Surgery. W. R. MacAusland Jr., J. J. Gartland and H. Hallock.—p. 604.
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Survey of Carpal and Tarsal Anomalies. R. O'Rahilly.—p. 626.
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Traumatic Subcutaneous Rupture of Tibialis Anterior Tendon. M. C. Mensor and G. L. Ordway.—p. 675.
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*Osteitis Pubis of Traumatic Etiology. R. J. Adams and F. A. Chandler. —p. 685.
Positive Pressure in Reduction of Fractures of Tibial Condyles: Preliminary Report. L. Spigelman.—p. 696.
Internal Fixation for Fractures and Dislocations of Pelvis. G. Whiston. —p. 701.
Flexorplasty of Elbow: Evaluation of Method. R. E. Carroll and J. J. Gartland.—p. 706.
Filum Terminale Syndrome (Cord-Traction Syndrome). G. J. Garceau. —p. 711.

Hyaluronidase in Traumatic Surgery.—Collections of extracellular fluid in the form of hematoma, hemarthrosis, and edema complicate many cases seen in orthopedic and traumatic surgery. Definitive treatment is often delayed while the surgeon waits for nature to dispose of hematoma and edema. The enzyme hyaluronidase is now available as a means to accelerate the dispersion of these fluids. Two years' experiences with this enzyme at the New York Orthopedic Hospital are reviewed in this report. Hyaluronidase acts by the depolymerization of the mucopolysaccharide hyaluronic acid. This acid forms the main constituent of connective tissue and joint fluid. The breakdown of these natural barriers facilitates rapid dispersion of extracellular fluid collections. The sprained ankle demonstrates the advantage of hyaluronidase therapy. The area of maximum swelling and its periphery are injected with 1,000 turbidity reduction units of the enzyme in 5 cc. of 1% procaine; an elastic bandage is applied and the patient is allowed to walk. One or two hours later, the swelling and hematoma are greatly reduced. The elastic bandage is then reapplied. By allowance of immediate painless weight-bearing, the disability time is greatly reduced. The efficacy of local anesthesia can be increased by the use of hyaluronidase, particularly in fractures about the forearm. Usually there is a 20 minute lag between injection and adequate anesthesia. By the addition of 500 turbidity reduction units of hyaluronidase to the procaine solution, excellent anesthesia is obtained in three to four minutes. Application of an elastic bandage enhances the action of the hyaluronidase in dissipating the hemorrhage and edema. With complete anesthesia and the reduction of the surrounding swelling, the bone ends are more easily palpated and a satisfactory reduction is possible. Hyaluronidase and procaine offer an effective nonoperative method to relieve the subfascial tension caused by edema and hemorrhage in supracondylar fractures of the elbow, which involve the threat of Volkmann's contracture. A case history is presented to illustrate this. Soft tissue hemorrhage, postoperative hematoma, and hemophylic hemarthrosis were other conditions in which hyaluronidase proved helpful. In a hemophiliac patient with an acute hemarthrosis, the clotting time and other laboratory data are obtained. Plasma or fresh blood is given to lower the clotting time. The joint is entered with a small bore needle, and 3 to 4 cc. of the viscid blood is removed. Then 1,000 turbidity reduction units of hyaluronidase are mixed with procaine in the amount equal to that of the blood withdrawn. This is injected into the joint and a snug elastic bandage is applied. No treatment other than bed rest is necessary. When the patient is reexamined in 24 hours, pain is usually absent and the range of motion is much greater. Occasionally, a second injection is necessary. After 48 hours, the patient can walk without pain or has free use of an upper extremity. This method produced favorable results in 19 of 20 cases of hemarthrosis.

Osteitis Pubis of Traumatic Etiology.—A review of the literature indicates that osteitis pubis is an inflammatory disease of bacterial origin that occurs most commonly following retropubic surgery in males. A youth with osteitis pubis was recently studied in the orthopedic surgery department of the University of Illinois hospitals. The uniqueness of this case and the review of four other very similar cases in the literature suggested that an entity similar to postoperative osteitis pubis in the elderly male may also occur in the younger age group. A youth, aged 18, was hospitalized with a history of lower midabdominal pain with radiation into the upper medial portions of the thighs. The onset had occurred one year previously while running in indoor track at high school. In January, 1949, his physician, suspecting appendicitis, removed the appendix, but upon resuming physical exertion the patient experienced a return of discomfort. The pain troubled him when he ran or walked, and he had a "waddling" gait when fatigued. In January, 1950, roentgenograms revealed a destructive lesion in the symphysis pubis. A biopsy was done, and a diagnosis of chondrosarcoma was made. The patient was then referred to the University of Illinois hospitals. Bony enlargement of the symphysis pubis was noted. Passive abduction of the hip joints beyond 20 degrees produced severe pain in the adductor groups and the symphysis pubis. In March, 1950, with a clinical diagnosis of chondritis of the symphysis pubis, a suprapubic resection of this structure was accomplished, the defect being bridged by an autogenous tibial-bone graft. At the time of surgery, the lesion appeared yellow in color, was firm and gritty in consistency, and contained irregularly arranged bony spicules. The suprapubic wound failed to heal, and within 10 days gross infection was evident. A hemolytic strain of Micrococcus pyogenes var. aureus (Staphylococcus aureus) was cultured from the pus. Neither penicillin nor streptomycin controlled the infection. Two months after its insertion, the bone graft and a sinus tract that communicated with the skin were removed surgically and the wound was packed open. Healing then occurred without sinus formation, and the patient was ambulatory six weeks later. He subsequently returned to full activity, including strenuous sports, without complaint or disability. A specimen for histological examination made possible a description of the pathological changes associated with osteitis pubis of traumatic origin in a young person. These findings suggest that the traumatic disease was inflammatory in nature and possibly bacterial in origin. Four similar cases from the literature are reviewed. Osteitis pubis of traumatic origin should be treated conservatively. Complete bed rest may be necessary in the acute phase and a plaster-of-Paris spica may be re-

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quired to limit hip and pelvic motion in such instances. Later, with improvement, a snugly drawn sacroiliac belt might be useful to decrease symphysial movement during weight-bearing. Ambulation should be resumed as soon as it can be tolerated, but strenuous activities should be minimized until roentgenographic and clinical signs indicate healing. The administration of antibiotics would probably be of value during the acute phase, especially if signs of gross infection become manifest. When abscess formation occurs incision and drainage should be done.

Journal of Immunology, Baltimore

71:119-168 (Sept.) 1953

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Interference Between Influenza and Equine Encephalitis Viruses in Tissue Culture. C. E. Taylor.—p. 125.
Growth Curve of Virus of Herpes Simplex on Chorioallantoic Membrane of Embryonated Hen's Egg. T. F. M. Scott, L. L. Coriell, H. Blank and A. Gray.—p. 134.
Inhibition by Lecithin and Cholesterol of Bacterial (Escherichia Coli) Hemagglutination and Hemolysis. E. Neter, N. J. Zalewski and D. A. Zak.—p. 145.
Influenza Virus in Allantoic Sac Tissue Culture: Quantitative Studies on Nucleic Acid Content During Growth and in Presence of Cortisone. C. R. Womack and E. H. Kass.—p. 152.

Journal of Investigative Dermatology, Baltimore

21:131-204 (Sept.) 1953

Temporary Depilation of Scalp Resulting from Use of New "Antifungal" Chemical. J. W. Wilson, H. Levitt, J. W. Carney and A. Yeaman. —p. 131.
Lichen Planus-Like Drug Eruption Due to Para-Amino Salicylic Acid: Report of 5 Cases, Two Showing Mouth Lesions. H. Shatin, O. Canizares and E. L. Worthington.—p. 135.
Distribution of Cholinesterases in Human Skin, with Special Reference to Eccrine and Apocrine Sweat Glands. H. J. Hurley Jr., W. B. Shelley and G. B. Koelle.—p. 139.
In Vitro Fungistatic Activity of Stilbamidine, Propamidine, Pentamidine and Diethylstilbestrol. F. C. Bocobo, A. C. Curtis and E. R. Harrell. —p. 149.
Dermatophyte, Microsporum Gypseum, as Saprophyte and Parasite. L. Ajello.—p. 157.
Observations on Cholinogenic Urticaria. J. K. Morgan.—p. 173.
Observations on Autosensitization in Contact Dermatitis. S. Epstein. —p. 183.
Course of Trichophyton Gypseum Infection in Rabbits Previously Infected with Trichophyton Purpureum: Effect of ACTH on Trichophytin Test. F. Reiss, E. M. Rosenbaum and L. Caroline.—p. 191.
Chemical Measure of Effect of Soaps and Detergents on Skin. E. J. Van Scott and J. B. Lyon.—p. 199.

Journal of Thoracic Surgery, St. Louis

26:221-330 (Sept.) 1953

Localization of Radioactivity in Lung and Lymph Nodes. J. R. Bryant, H. F. Berg and W. M. Christophersen.—p. 221.
Ability of Pulmonary Vascular System to Influence Spread of Tumor Emboli. E. A. Lawrence, D. B. Moore and G. I. Bernstein.—p. 233.
Bronchial Resection and Anastomosis. P. W. Gebauer.—p. 241.
Pulmonary Distension as Seen in Lordotic Roentgenogram. J. Gordon and W. B. Zinn.—p. 261.
Experimental Lung Transplantation. W. B. Neptune, R. Weller and C. P. Bailey.—p. 275.
*Resection of Acquired Coarctation of Low Thoracic Aorta and Replacement with Preserved Vessel Graft. R. A. Deterling, Jr.—p. 290.
*Surgical Closure of Interauricular Septal Defects. V. O. Björk and C. Crafoord.—p. 300.
Thoracoabdominal Ectopia Cordis. J. W. Major.—p. 309.
Chronic Chylothorax Associated with Hygroma of Mediastinum. A. S. W. Touroff and G. P. Seley.—p. 318.
Traumatic Chylothorax Following Esophageal Resection. S. Bressler, D. Wiener and S. A. Thompson.—p. 321.
Localized Pleural Mesothelioma of Epithelial Type. R. Yesner and A. Hurwitz.—p. 325.

Resection of Acquired Coarctation.—The coarctation commonly treated by surgery occurs as a congenital anomaly immediately below the origin of the left subclavian artery. In the case reported, a coarctation that was thought to be acquired was located 6 cm. above the diaphragm. While surgical repair of coarctation occurring in the usual site is no longer considered rare, only five operations have been performed and reported in patients with stenosis just above the diaphragm. In a 23-year-old woman with a long coarctation of the low thoracic aorta, a 9 cm. segment was excised and replaced by an 8 cm. preserved aortic homograft. An obliterated left subclavian artery was found. A left hemothorax occurring on the fourth postoperative day was believed to be due to a leak from an aortic fracture caused by the proximal aortic clamp. The end-result was quite satisfactory, with complete resolution of the hemothorax and normal brachial blood pressure and blood flow to distal extremities. The character and site of the lesion, as well as the medical history, support the theory that the coarctation was acquired.

Closure of Interauricular Septal Defects.—This new and successful method for the closure of interauricular septal defects is an elaboration of the one described by Söndergaard in 1952. A groove is made between the superior vena cava and pulmonary veins. With a finger inserted in the auricle through the right auricular appendage, a needle is guided subendocardially in the septal plane. It is introduced through the right auricular wall close to the root of the aorta just behind the right coronary artery. The needle follows the aorta down and through the upper portion of the interventricular septum. Through the posterior portion of the interventricular septum the needle should come more toward the left side and then out through the left auricular wall behind the inferior vena cava, close to the annulus fibrosus. The two ends of the suture are tied in the groove. This method seems to be applicable even in patients with a very large interauricular septal defect without a septal rim.

Journal of Urology, Baltimore

70:343-558 (Sept.) 1953. **Partial Index**

Surgical and Hormonal Therapy of Benign and Malignant Androgenic Hyperfunction of Adrenal Cortex. C. V. Hodges.—p. 343.
Infarcts of Kidney. J. S. Fitzgerald and P. S. Mullins.—p. 352.
Calyceal Diverticula or Pyelogenic Cysts. R. G. Wyrens.—p. 358.
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Facilitation of Passage and Extraction of Ureteral Calculi. E. F. Nation. —p. 373.
New Ureteroplasty: Advancement of Ureter by Vesico-Ureteral Pedicle Graft. R. B. Higgins.—p. 376.
Transperitoneal Approach to Lesions of Lower Ureter. B. R. Sears and J. W. Schulte.—p. 386.
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Lymphangioma of Ureter. F. B. Jeppesen.—p. 410.
Re-Implantation of Ureters into Bowel Following Cutaneous Ureterostomy for Disruption of Ureterosigmoidostomy. C. K. Pearlman. —p. 415.
Leakage and Reflux in Uretero-Intestinal Anastomosis: I. Free Peritoneal Graft. F. Hinman Jr.—p. 419.
Experimental Ureteral Transplants to an Ileal Segment Anastomosed to Rectum. L. W. Riba, C. Tsai and W. G. Maddock.—p. 426.
Autogenous Vein Grafts and Venous Valves in Ureteral Surgery: Experimental Study. M. L. Rosenberg and G. A. Dahlen.—p. 434.
Study of Hydrodynamics of Upper Urinary Tract Following Ureterosigmoidostomy. C. F. Rusche and W. C. Cook.—p. 447.
Surgical Technique for Stress Incontinence in Women: Modification of Millin's Technique. F. Barquín, A. Peréira and L. Bay.—p. 454.
Massive Electrocoagulation of Deeply Infiltrating Bladder Tumors Combined with Ligation of Vena Cava for Prevention of Pulmonary Embolism. F. E. B. Foley, E. J. Richardson, W. P. Mulvaney and I. Victor.—p. 456.
Carcinoma of Bladder: Review of 104 Cases from 1942 to 1952. C. P. Mathé and M. A. Llanos.—p. 464.
Rhabdomyosarcoma of Bladder: Review and Report of Case. H. I. Riddell and H. G. Kudish.—p. 472.

Louisiana State Medical Society Journal, New Orleans

105:293-328 (Aug.) 1953

*Massive Melena: Survey of 129 Cases Seen at Charity Hospital from March, 1950, to December, 1952. J. D. Rives and R. O. Emmett. —p. 293.
Electrocardiographic Changes with Spontaneous Mediastinal Emphysema. J. E. Holoubek and E. R. Moser.—p. 299.
*Heart Disease in Chronic Arsenic Poisoning: Clinical Report of Two Cases. R. L. Robbins.—p. 301.
Diagnosis of Tuberculosis by Isolation of M. Tuberculosis in Yolk Sack of Chick Embryo. G. J. Buddingh and J. W. Brueck.—p. 304.
Corneal Transplants. G. M. Haik.—p. 308.
Nature and Management of Cardiac Arrest. P. T. DeCamp.—p. 311.
Psychiatry and Public Opinion. R. C. Young.—p. 318.

Massive Melena.—Of 4,377 patients admitted to the surgical services of the Charity Hospital at New Orleans for acute abdominal complaints, 380 (8.7%) were emergency admissions for sudden hemorrhage from the gastrointestinal tract. Of the latter group, 251 patients (66%) had hematemesis with or without melena; 129 (34%) had melena alone. These 129

cases form the basis of this report. From observations on these patients a procedure was evolved which is now followed when a patient presents himself with a story of bleeding from the rectum. First the constitutional effect of the hemorrhage, that is, the blood pressure and evidence of shock are ascertained. Blood transfusions are instituted if shock exists. A digital examination of the rectum determines whether blood is present there. If the cause of hemorrhage is not obvious, a Levine tube is inserted into the stomach to determine whether blood can be found in the upper gastrointestinal tract. Physical examination is limited to a superficial examination of the heart and lungs, measurement of blood pressure, and palpation and auscultation of the abdomen. Leukemia should be looked for. A red blood cell count and a hematocrit will indicate roughly the amount of blood loss. A nonprotein nitrogen or a blood urea nitrogen determination is made for evidence of uremia. These tests are likely to show high values in the presence of large quantities of blood in the gastrointestinal tract; however, they are not usually high enough to confuse the diagnosis with that of true uremia. If the evidence points to bleeding from the upper gastrointestinal tract, x-ray studies of the gastroduodenal segment should be considered, even during the bleeding period. Until recently the authors avoided such examinations, but they have real value, although the gastrointestinal tract containing blood clots may not give clear pictures. If the evidence points to a lesion below the gastroduodenal segment, sigmoidoscopic examination should be done. A barium enema should be given, if none of these examinations demonstrate the location of the bleeding. Massive bleeding from the rectum is not characteristic of carcinoma, the lesion is more likely to be diverticulosis and diverticulitis. It may be wise to defer the examination by barium enema if evidence of acute diverticulitis is present. Surgery may be necessary if the diagnosis cannot be established by other means, although it is unreliable for determining the location of gastrointestinal bleeding. Roentgen examination is the best method for locating lesions that cause melena, especially in the gastroduodenal segment. It is almost equally valuable in the colon above the rectosigmoid junction. Most lesions that are readily demonstrable by roentgenograms in the colon do not usually produce gross hemorrhage. Proctoscopic examination, or rather sigmoidoscopic examination, is practically infallible in lesions of the rectum and rectosigmoid junction.

Heart Disease in Chronic Arsenic Poisoning.—Robbins presents the histories of two patients with chronic arsenic poisoning. The first patient, a cotton farmer, gave a history of having dusted cotton repeatedly from 1923 through 1939 with a compound that contained arsenic, and during those years he had recurrent episodes of vertigo, weakness, nausea, and vomiting. In 1946, he again was briefly exposed to arsenic, and these symptoms recurred and were followed by sore throat, hoarseness, swelling of the face and neck, and paroxysmal dyspnea. Edema of the soft palate and of the pharynx was discovered, and although diphtheria organisms could not be found, he was treated with digitalis, pencillin, and diphtheria antitoxin. An x-ray film of the chest revealed pulmonary congestion. From 1947 through 1952, the patient was hospitalized 19 times, but he never fully recovered from the episode in 1946. Serial electrocardiograms showed myocardial disease. The second patient was a 40-year-old laborer, whose job required that he clean oil-well drilling equipment. He would mix a powder with water, place this solution in a closed container, light a fire under it, and expose the tools to the steam, previously treated with a compound of hydrochloric acid and arsenic. After having been thus employed for about eight months, he noted nausea, vomiting, anorexia, giddiness, and excessive salivation. Two months later an erythematous eruption developed about the hands and feet, associated with paresthesia. The rash spread until it involved his entire body. Conjunctival erythema and lacrimation developed. In May, 1949, he was found to have a generalized scaling pigmented maculopapular rash, with marked thickening of the palms and soles. A Kolmer blood test for syphilis was positive. In September, 1950, the burning pains in the feet had gotten worse until he could no longer stand or walk. He again had nausea, vomiting and abdominal distress. His gums were swollen and painful, and his teeth loose. The hair and nails were found to contain 33.9 parts per million of arsenic, and 24 hour urine specimen contained 0.006 parts per million of arsenic. Treatment consisted of bed rest, penicillin, and dimercaprol. There was slight improvement in the paresthesia and the cardiac size diminished. He was discharged with the diagnosis of chronic arsenical intoxication. In October, 1951, he was hospitalized because of recurrence of all symptoms, after having returned to his old job. He received dimercaprol together with a high caloric diet and multiple vitamins, but his clinical response was not gratifying. He was again hospitalized in March, 1952, because of ascites, pedal edema, abdominal cramps, diarrhea, chronic cough, exertional dyspnea, and palpitations. He responded fairly well to digitalis, low sodium diet, and mercurial diuretics. He was followed in the outpatient clinic, and six months later symptoms of chronic congestive failure persisted. The etiology of the heart disease in these men was never explained. Neither patient had hypertension, retinopathy, nor evidence of valvular pathology; both had congestive rather than anginal failure. Although in one patient the serologic tests for syphilis were positive, the absence of clinical and radiographic evidence of valvular and aortitic lesions precluded the diagnosis of syphilitic heart disease. The pharyngeal edema, which suggested diphtheria, was the most classic symptom of early chronic arsenical intoxication.

Medical Annals of District of Columbia, Washington

22:449-516 (Sept.) 1953

*Gastric Decompensation. W. T. Gibb Jr.—p. 449.
Management of Essential Hypertension. J. M. Evans.—p. 456.
X-Ray Examination of Gallbladder. W. W. Stanbro.—p. 459.
Artificial Insemination. R. Bieren.—p. 461.
Anxiety Reactions: Acute Anxiety Attack or Panic, Anxiety and Tension States, and Anxiety Neurosis: Outline of Data Relative to Their Identification and Management. H. P. Laughlin.—p. 463.

Gastric Decompensation.—According to Gibb there are certain aspects of prolonged duodenal ulcer that are not clearly explainable by the usually accepted concepts of the mechanism involved. It is usually assumed under these circumstances that the lumen of the pylorus is occluded by scarring and contraction, by edema associated with an antral gastritis or duodenitis, spasm, or combinations of all three. The fact that retention can be relieved in most cases by bed rest, antispasmodics, diet, and repeated gastric lavage leads to the conclusion that edema is largely responsible. The author examined with the flexible gastroscope the stomachs of many persons with varying degrees of gastric retention, and, except for some with maligiant lesions, he has yet to see a single pylorus that was actually stenosed or occluded or an antrum that was edematous to a degree sufficient to produce occlusion. Before presenting his somewhat different concept of the pathophysiological mechanism of pyloric obstruction and prolonged gastric retention, he presents his idea of the normal functioning of the stomach and duodenum. In cases of repeated ulcerations at the duodenal cap more and more scar tissue forms and gradually the cap loses its normal elasticity. The intraduodenal pressure regulatory mechanism fails, and, when the pylorus opens after systole, an abnormal amount of reflux occurs. In addition, the lumen of the very first portion of the duodenum is reduced because of scar tissue. Greater force is required to get the usual amount of material through it in the usual length of time. The same situation may be said to exist as in a stenosed and incompetent heart valve. Similar to the heart, the stomach has to work harder in order to keep up with its full work load. Unlike the heart, however, the stomach has no capacity to hypertrophy to assist it in remaining competent. If at this point the work load of the stomach is decreased, as, for example, when the patient goes on a voluntary or prescribed diet that reduces the quantity and changes the character and consistency of the food he eats, the stomach may be able to maintain its compensation and empty in the prescribed length of time. The clinical picture of pyloric stenosis is not due to actual closure of the pylorus, but rather to a relative incompetence of its valve action. Because the competence of the mechanism can be restored by such simple means as repeated gastric lavage does not mean that the

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underlying pathological condition causing the situation has in any way been changed. This concept may explain why pyloroplasty does not always work as well as might be expected. The author admits that the evidence to support his concept of gastric compensation and decompensation is fragmentary, open to criticism, and may be incorrect. He feels, however, that it is a more workable theory than any that are described in the standard textbooks.

Medicine, Baltimore

32:293-388 (Sept.) 1953

Nutritional Influences on Physiology of Skin: Observations on Metabolism of Vitamin A. R. D. Griesemer, C. N. Frazier and I. H. Blank. —p. 293.
Nature and Treatment of Polycythemia: Studies on 263 Patients. J. H. Lawrence, N. I. Berlin and R. L. Huff.—p. 323.

Metabolism, New York

2:391-484 (Sept.) 1953

Body Compartments: Their Measurement and Application to Clinical Medicine. G. J. Hamwi and S. Urbach.—p. 391.
*Maintenance Management of Addison's Disease with Injections of "Long-Acting" Microcrystalline Esters of Desoxycorticosterone. S. Z. Sorkin and L. J. Soffer.—p. 404.
Case of Hyperadrenocorticism with Spontaneous Improvement: Effects of Potassium Acetate, Corticotropin (ACTH), Cortisone Acetate, Desoxycorticosterone Acetate and Methyltestosterone. G. W. Liddle, J. E. Giansiracusa and L. L. Bennett.—p. 411.
Modification of "Steroid Diabetes" by Potassium. L. W. Kinsell, H. E. Balch and G. D. Michaels.—p. 421.
Effect of ACTH on Responsiveness to Insulin. H. J. Zimmerman, A. E. Parrish and L. K. Alpert.—p. 424.
Metabolism of Intravenously Infused Fructose in Man. T. E. Weichselbaum, H. W. Margraf and R. Elman.—p. 434.
Role of Human Liver in Assimilation of Intravenously Administered Fructose. A. I. Mendeloff and T. E. Weichselbaum.
Utilization of Intravenous Fructose in Diabetic Acidosis and in Pancreatectomized Human. W. H. Daughaday and T. E. Weichselbaum. —p. 459.

Maintenance Management of Addison's Disease.—An attempt was made to improve the administration of desoxycorticosterone acetate (DCA) in the maintenance therapy of Addison's disease, with a view toward long-term management. Formerly, the two methods of administration were daily injection in an oil solution and annual or semiannual implantation of the crystalline hormone in the form of pellets. The latter method was designed for long-term therapy, but was found technically impractical. The successful use by injection of suspensions of crystalline sex hormones, which are absorbed slowly and thus give a prolonged effect suggested to Meier, Gasche, and Frey that crystalline desoxycorticosterone acetate might be used in a similar manner. A test of this idea was run on 10 patients with Addison's disease, after the above authors' experiments on dogs and rats whose adrenals had been removed had proved successful. The maintenance treatment was carried out successfully with aqueous suspensions of microcrystalline desoxycorticosterone trimethylacetate and phenylacetate given in injections of 50 to 120 mg. at intervals of four to six weeks. All of the patients received small daily supplements of sodium chloride, and two patients were also given cortisone acetate.

Military Surgeon, Washington, D. C.

113:157-250 (Sept.) 1953

Ship's Motion and Incidence of Seasickness. S. W. Handford, T. E. Cone Jr. and S. C. Gover.—p. 157.
Evacuation by Army Aviation During Exercise Long Horn. D. E. Liston and C. G. Giesecke.—p. 167.
ACTH and Cortisone Abstinence Syndrome. R. de R. Barondes, T. J. Kane and C. Strachan.—p. 171.
Endemic Panmyelotoxicosis in Russian Grain Belt: Part One: Clinical Aspects of Alimentary Toxic Aleukia (ATA); a Comprehensive Review. C. F. Mayer.—p. 173.
Informal Report on Use of Dark Field in Diagnosing Jaundice. C. A. Toledo S.—p. 189.
Open Reduction of Fracture of Edentulous Mandible. R. E. Crowley. —p. 195.
Flight Nurse as Leader. F. I. Lay.—p. 196.
Survey of Intestinal Parasitic Infection Found in Feces of Formalin-Fixed Appendices. M. B. Rodney, B. Sonnenberg and R. R. Dalton. —p. 200.
Shrapnel. J. H. Schaefer.—p. 206.
Trans-Medic Team. W. G. Newbold.—p. 208.

Minnesota Medicine, St. Paul

36:897-1008 (Sept.) 1953

Problems in Roentgen Diagnosis of Bleeding Lesions of Upper Gastrointestinal Tract. J. C. Bell.—p. 917.
Massive Upper Gastrointestinal Hemorrhage. J. M. Dorsey.—p. 921.
*Peptic Ulcer Problem. O. H. Wangensteen.—p. 924.
Male Sterility. H. J. Walder.—p. 935.
Evaluation of Female Sterility. L. L. Freidman.—p. 938.
The Minnesota Medical Profession and Tuberculosis. J. A. Myers. —p. 944.
Extrapulmonary Intrathoracic Tumors: Clinical Manifestations and Surgical Treatment. S. W. Harrington.—p. 953.
Aspiration Biopsy of Bone Marrow: Its Diagnostic Value. G. L. Pease. —p. 961.

Peptic Ulcer.—According to Wangensteen, peptic ulcer is still a challenging problem. Patients who get along well on medical management are not candidates for surgery. The patient to whom the monotony of the ulcer diet does not appeal, the patient who is never long wholly free from pain, the patient with recurrent gastric hemorrhage, as well as the patient with periodic episode of obstruction—all should be advised to have an operation for the relief of peptic ulcer. There seems to be no reason to withhold operation from patients who have had more than one episode of hematemesis from peptic ulcer. When the medical profession learns to manage the threat of hemorrhage from peptic ulcer in a satisfactory manner, the mortality will disappear. The serious threat of perforation is now largely under control. Through improved surgical care, including employment of antibiotics and better toilet of the peritoneal cavity at the time of the closure of the perforation, the mortality of perforation is no longer as serious as it was a decade ago. Earlier and more frequent recourse to operation is particularly advisable for gastric ulcers, inasmuch as they frequently recur at the same site and involve the threat of cancer. The author concludes that the key to the reduction of the high mortality of peptic ulcer in patients between 40 and 70 is readier recourse to operation in patients who have had gastric hemorrhage, which must be recognized as synonymous with failure of adequate control by conservative means. Hemorrhage is the most important single cause of death from peptic ulcer.

Nebraska State Medical Journal, Lincoln

38:313-352 (Sept.) 1953

Rehabilitation: Third Phase of Medical Care. H. N. Neu.—p. 315.
Psychosomatic Medicine—New Approach. F. R. Barta.—p. 320.
Preventive Care of Infants and Children: III. Influence of "Guided Growth" on Feeding and Sleeping Patterns of Infants—Physiological and Psychological Background. B. B. Oberst, C. A. Tompkins and V. J. P. Hamlin.—p. 324.
Disposition of Ulcer in Surgery for Duodenal Ulcer. B. R. Bancroft. —p. 329.
Special Poliomyelitis Clinic. E. W. Hancock.—p. 331.
Viruses as Cause of Cancer. H. E. Eggers.—p. 334.

New England Journal of Medicine, Boston

249:245-386 (Aug. 27) 1953

*Toxoplasmosis. R. S. Beckett and F. J. Flynn Jr.—p. 345.
Psychiatric Research in a General Hospital. H. M. Fox.—p. 351.
The Theory and Practice of Public Health. V. A. Getting and C. F. Ryder.—p. 354.
Functional Disorders of Menstruation in Adolescence. J. W. McArthur. —p. 361.
Anaphylactoid Reaction to the Hydriodide of Diethylaminoethyl Ester of Penicillin G (Neo-Penil). B. T. Fein.—p. 368.

Toxoplasmosis.—Toxoplasmosis has been recognized for about 50 years, and an increasing number of cases of it in humans is being reported. The authors report two new cases of congenital toxoplasmosis, one of which closely resembled erythroblastosis fetalis. It is suspected that the infection was transferred to the mother by a dog. Involvement of the placenta was demonstrated in the second case. A classification of the disease is set up which includes six types: (1) asymptomatic infection, (2) mild grippe-like infection, (3) infections simulating infectious mononucleosis, (4) chorioretinitis, (5) acquired systemic infection, and (6) congenital infection. Serologic tests such as the Sabin-Feldman dye test are used to increase and improve the diagnosis of toxoplasmosis, but effective treatment of toxoplasma infections is still needed.

New Jersey Medical Society Journal, Trenton

50:363-442 (Sept.) 1953. **Partial Index**

Public Relations: New Old Concept. R. I. Nevin.—p. 370.
Trends in Medical Care: Medical Service Plans in New Jersey. E. W. Sprague.—p. 371.
Half Century of Medicine. G. H. Lathrope.—p. 377.
Fifty Years of Surgical Progress. D. B. Allman.—p. 382.
Advances in Maternal Welfare: 1903-1953. H. P. Shipps.—p. 391.
Military Role of New Jersey Physicians in Past 50 Years. H. A. Brodkin. —p. 394.
Mother's Milk Bank of Essex County. H. A. Murray.—p. 401.
Fifty Years of Pharmacology. R. D. Goodman.—p. 405.
Fifty Years of Progress in Public Health. D. Bergsma.—p. 417.
Fifty Years of Urology: Review. C. R. O'Crowley.—p. 427.

Ohio State Medical Journal, Columbus

49:769-860 (Sept.) 1953

*Bronchiogenic Carcinoma Simulating Virus Pneumonia. H. R. Custer and K. P. Klassen.—p. 793.
Practical Aspects of Burn Therapy. E. H. Ellison, R. D. Williams and R. M. Zollinger.—p. 798.
Use of Split-Thickness Skin Grafts in Bilateral Ischiorectal Abscess. F. J. Rack.—p. 802.
Brain Wave Patterns and "Crystallized Experiences." D. M. Palmer and H. A. Rock.—p. 804.
Curb Service for Diagnosis: Mobile Laboratory. I. C. Albert.—p. 807.

Bronchogenic Carcinoma Simulating Virus Pneumonia.—Custer and Klassen show that bronchogenic carcinoma may at first produce bronchial stenosis and partial occlusion with associated pneumonia peripherally, which will respond temporarily to antibiotic therapy. However, as the cancer grows the bronchus becomes completely obstructed, resulting in recurrent pneumonitis or atelectasis which is mistaken for pneumonia. This is the type which is erroneously diagnosed as recurrent or virus pneumonia. Three case histories are presented which show the danger of making a diagnosis of virus or recurrent pneumonia. The first of these patients was treated for pneumonia by several physicians over a period of nine months. His history was compatible with, but not diagnostic of, pulmonary cancer. The correct diagnosis was not established. The second case is of interest because the history, the physical examination, and an extensive diagnostic search gave no indication of bronchogenic carcinoma. This case also demonstrates that occasionally it is extremely difficult to diagnose the cancer grossly even when the surgeon has the lung exposed. In the presence of diffuse inflammatory necrosis the frozen section reports are often misleading and the decision rests entirely with the judgment and experience of the thoracic surgeon. The third patient had had signs of a pulmonary lesion for many years and progressive symptoms with repeated bouts of pneumonia for over a year. A pulmonary malignancy was not considered until the bronchus had been completely occluded. This case demonstrates the fatality of procrastination. The authors stress that any patient with pneumonia who does not respond to antibiotic therapy within three weeks should be suspected of having either a Friedlander pneumonia, lung abscess, tuberculosis, or bronchial obstruction. All efforts should be made to arrive at the correct diagnosis as early as possible, and any patient in whom bronchogenic carcinoma cannot be excluded by other means is entitled to an exploratory thoracotomy.

Pennsylvania Medical Journal, Harrisburg

56:769-864 (Sept.) 1953

Surgical Treatment of Peripheral Vascular Disease. C. A. Hatfield. —p. 793.
Treatment of Mental Disorders in Geriatric Patient. D. V. Conwell and C. J. Kurth.—p. 794.
Rehabilitation After a Stroke. M. B. Ferderber.—p. 798.
What is General Practice. J. H. Nagler.—p. 804.
New Technique in Control of Postoperative Anorectal Pain: Study of 200 Patients. E. J. Lowell Jr., H. E. Bacon and H. D. Trimpi.—p. 807.
Use of Polyvinylpyrrolidone in Management of Shock-Like States: Report of Case. C. L. O'Connell Jr., D. P. Greenlee and F. T. Herron. —p. 813.
Compression of Duodenum by Superior Mesenteric Artery. M. Shumway, W. M. Uhler and P. L. Davis.—p. 816.

Rocky Mountain Medical Journal, Denver

50:703-776 (Sept.) 1953

Presidential Address: E. J. Guilfoyle.—p. 725.
Clinical Note. O. S. Budge.—p. 727.
Psychiatric Difficulties Associated with Eating. C. H. H. Branch and D. E. Reiser.—p. 728.
Danger of Peptic Ulcer Complications During Cortisone or ACTH Therapy. J. A. Edwards and G. F. Wollgast.—p. 734.

50:777-842 (Oct.) 1953

Heart Disease in Small Infants and Children. F. H. Adams.—p. 799.
Problem of Appendicitis in Colorado: Mortality Study. M. E. Peck, J. A. Lichty and A. E. Prevedel.—p. 803.
Use of Bedside Laboratory in Establishing and Maintaining Fluid and Electrolyte Balance. J. R. Spencer and K. C. Sawyer.—p. 808.
Health for You and You for Health. F. S. Crockett.—p. 810.

South Carolina Medical Assn. Journal, Florence

49:227-256 (Sept.) 1953

*Poisoning Due to Anticholinesterase. V. Moseley and H. P. Snead. —p. 227.
Cretinism and Childhood Myxedema. C. R. Holmes and G. W. Smith. —p. 232.
Prevention of Rheumatic Fever. M. T. Bellows, E. E. Fischel, A. Kuttner and others.—p. 239.
William Osler's Continuing Influence in Field of Medicine. J. H. Gibbes. —p. 240.

Poisoning Due to Anticholinesterase.—Three cases of poisoning that resulted from anticholinesterase insecticides are described in men between the ages of 18 and 37. Two of the patients were employed by a chemical plant and had been exposed to tetraethylpyrophosphate. Both these men had constricted fields of vision and inspiratory and expiratory wheezes over both lung fields. Although the patients wore full protective equipment, observed the safety rules, and did not knowingly come in direct contact with tetraethylpyrophosphate, the authors felt that their symptoms were undoubtedly due to poisoning with this insecticide. The patients were given 1 mg. of atropine subcutaneously on admission, and after two hours this dose was repeated. Elixir of terpin hydrate was given for the cough. All the symptoms subsided within a few hours. No symptoms had reappeared within 24 hours, and the patients were discharged improved. The early recognition of tetraethylpyrophosphate poisoning and prompt treatment resulted in only minor morbidity. The third patient, a farmer, had sprayed tobacco with parathion for four hours. Within one hour he complained of muscle cramps, nausea, sweating, and cough. Shortly afterward he became irrational. He was given 1 mg. of atropine subcutaneously twice on the way to the hospital and was admitted in a semicomatose state. The history revealed that the patient had sprayed tobacco with parathion for a period of about four hours two weeks previously. His only protection against parathion on both occasions was a handkerchief tied over his nose. During the first two hours in the hospital he received 12.2 mg. of atropine without signs or symptoms of toxicity; following subsequent administrations, he became restless and that was attributed to stimulation of the central nervous system by atropine. This undesired side-effect was controlled with phenobarbital sodium, and the dose of atropine was regulated according to the size and reaction of the pupils and flushing of the skin. The patient was given 0.5 gm. of dihydrostreptomycin and 400,000 units of procaine penicillin every 12 hours prophylactically for the first six days of his hospital stay in order to guard against pulmonary infection. After regaining consciousness 72 hours after admission, the patient had no recurrence of previous symptoms and no new symptoms during the following five days of observation. The mechanism of action of the tetraethylpyrophosphate and parathion is by irreversible combination with cholinesterase in all tissues of the body resulting in an excess of acetylcholine, with symptoms depending quantitatively on the amount of cholinesterase inhibited. The danger of additive toxic effects from repeated exposures to small amounts of these insecticides is stressed because of the slow rate of restoration of cholinesterase activity to normal levels. Safety recommendations for workers handling the anticholinesterase insecticide are listed.

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Southern Medical Journal, Birmingham, Ala.

46:837-936 (Sept.) 1953. **Partial Index**

*Intravascular Hemolysis: Morphologic Study of Schizocytes in Thrombotic Purpura and Other Diseases. W. M. Monroe and A. F. Strauss.—p. 837.
Variety of Spinal Lesions Simulating Disk Syndrome. F. J. Otenasek.—p. 843.
Indications for Bone Grafting in Primary Treatment of Fractures. K. A. Fischer and K. D. Leatherman.—p. 846.
Fractures of Head of Radius. C. J. Frankel.—p. 851.
Premature Closure of Cranial Sutures. J. D. King, J. H. Patterson and W. W. Bryan.—p. 852.
Management of Chronic Maxillary Sinusitis in Children. F. L. Bryant.—p. 856.
Evaluation of Pulmonary Insufficiency in Asthma, Pulmonary Fibrosis, and Other Types of Chronic Lung Disease. K. T. McKee.—p. 859.
Psittacosis Problem in Florida. L. L. Parks.—p. 864.
Clinical Aspects of Esophageal Hiatus Hernia: Association of Other Diseases in 158 Cases. J. O. Burke, K. Plummer and C. Robinson.—p. 887.
Torticollis: Its Dynamics and Therapy. R. W. Garnett Jr. and K. Elbirlik.—p. 892.
Thyroid Extract and Its Effect on Ovulation and Menstruation: Clinical Study of 38 Cases with Some Laboratory Data. W. O. Johnson and J. T. Bradbury.—p. 898.
Thyroid Crisis Treated with Corticotropin. A. M. Freeman and H. L. Holley.—p. 905.
Pituitary Necrosis: Following Osteomyelitis of Sphenoid Bone. N. F. Coulter and D. A. J. Morey.—p. 907.
Torsion of Spermatic Cord. R. B. Carson.—p. 909.
Etiology of Hypertension in Coarctation of Aorta. R. C. Little.—p. 911.
Use of Aerosol Trypsin in Atelectasis Neonatorum. E. Balthrop and L. Hicks.—p. 914.
Clinical Evaluation of Disc Method for Determination of Bacterial Sensitivity to Antibiotics. P. B. Holliday Jr.—p. 916.
Improved Friedman Pregnancy Test. J. C. Norris and J. Spink.—p. 919.

Intravascular Hemolysis.—Two fatal cases of thrombotic, thrombocytopenic purpura are reported in a 22-year-old man and in a 62-year-old woman. In the man the disease was of relatively long duration, representing the chronic type, while the woman had the acute type of the disease. Necropsy revealed extensive thromboses in the myocardial vessels of both patients. In both cases, appreciable numbers of erythrocyte fragments were observed at the site of the changes in the myocardial vessels, varying from barely visible granules taking a positive stain for hemoglobin to cells about half the diameter of a red cell. The kidney of the woman, which had many thrombi, showed many of these cell fragments, while in the man there were neither renal thrombi nor erythrocyte fragments. These tiny cell fragments, which often had the full hemoglobin content of a normal erythrocyte, must have arisen by fragmentation of larger cells without loss of the pigment. The term schizocytes has been coined in 1892 by Ehrlich for these small red cells; they were counted by the authors in 40 consecutive suitable unselected necropsies. Organs examined were heart, lung, liver, spleen, pancreas, adrenal, and kidney. The myocardium contained the highest number in 23 cases and the second highest in 2. The kidney was highest in three, and second highest in seven. The authors believe that the myocardial vessels may be a prominent site of mechanical red cell destruction by fragmentation, thus ascribing a new functional role to the coronary circulation. The anemia in thrombotic, thrombocytopenic purpura may be caused by mechanical red cell destruction, especially at the site of vascular lesions.

Virginia Medical Monthly, Richmond

80:477-544 (Sept.) 1953

Duodenal Ulcer. H. H. Bradshaw.—p. 481.
Treatment of Coarctation of Aorta with Homologous Graft—Report of Case. L. H. Bosher Jr.—p. 487.
*Bilateral Total Adrenalectomy in Treatment of Carcinoma of Prostate. K. E. Blunden, R. C. Bunts and F. A. Wade.—p. 492.
Medical Profession and Public Health. J. L. Hamner.—p. 499.

Bilateral Total Adrenalectomy in Carcinoma of Prostate.—Removal of the adrenal glands, which are known to be responsible for five-eighths of the output of androgens, is an antiandrogenic measure and like other antiandrogenic measures (orchiectomy and estrogen therapy) it has a beneficial effect in metastatic disease of the prostate. Actual temporary regression of the disease at a period when extension rather than regression is to be expected has been demonstrated in some cases. Pain is relieved, and the patient's well-being is increased. Maintenance can be satisfactorily achieved with cortisone, and elaborate laboratory control is not needed. The effect of the procedure on life expectancy cannot be determined at this time, because all the reports made so far have been preliminary in nature and nearly all the patients subjected to adrenalectomy have been in the terminal stage of the disease. The only indications justifying the procedure at present are clinical evidence of advanced active metastatic cancer, loss of response to both estrogen therapy and orchiectomy, and incapacitating pain or debility. The benefit afforded by the removal of androgenic elements in hopelessly advanced cases, however, suggests that early adrenalectomy may prove valuable in the treatment of early prostatic cancer. Dramatic relief of pain was secured by this procedure in two patients with advanced metastatic disease, one of whom was discharged on the 14th postoperative day with the expectation that he would soon be able to return to work. The other, who was partially paraplegic, was greatly improved and remained free from pain for the first three months. Pain then gradually recurred but was relieved by cordotomy at the D-2 level.

Western J. Surg., Obst. & Gynecology, Portland, Ore.

61:491-558 (Sept.) 1953

*Bilateral Adrenalectomy in Treatment of Advanced Neoplastic Disease. W. F. Barker, E. T. Yuhl, J. M. Beal Jr. and others.—p. 491.
Cystic and Cavernous Lymphangioma. J. D. Briggs, F. Leix, W. H. Snyder Jr. and L. Chaffin.—p. 499.
Clinical Study of 56 Duodenal Tumors. E. J. Joergenson, L. A. Weibel and L. E. Keasbey.—p. 507.
Malignant Melanoma: Critical Review of Surgical Problems. L. Dobson and R. A. Walsh.—p. 518.
Pulmonary Embolism. J. M. Farris.—p. 524.
Vital Staining of Lymphatics in Surgery of Carcinoma of Large Intestine. J. Weinberg and H. J. Movius II.—p. 528.
Value of Early Neurolysis in Contused Injuries of Peripheral Nerves. H. A. Brown.—p. 535.
Direct Intracardiac Surgical Relief of Pulmonary Stenosis. W. H. Muller Jr., J. F. Dammann Jr. and W. P. Longmire Jr.—p. 538.
Biological Predeterminism in Gastric Carcinoma: Limiting Factor in Surgical End-Results. I. Macdonald.—p. 547.

Bilateral Adrenalectomy in Patients with Advanced Neoplasms.—The authors report the results of removal of the adrenals and of castration in nine patients with advanced neoplastic disease who had been previously treated by surgery, irradiation, and hormone therapy. Transabdominal bilateral adrenalectomy through a long, curved transverse upper abdominal incision was performed in three patients with melanoma in whom orchiectomy was also performed at the same time. The course of the disease was not altered, and the patients died six, three, and two months after the intervention. The same approach was used in three patients with carcinoma of the breast whose ovaries were removed through the same incision. Pain was relieved in these patients who are still living, although the survival periods of six, five, and one months are too short to be significant. Pain was relieved in only one of three patients with carcinoma of the prostate. The initial treatment in these patients consisted of transurethal prostatectomy, orchiectomy, and estrogen therapy. Two have died seven and three months after adrenalectomy was performed through separate extraperitoneal flank incisions in one stage. The third is still alive six weeks after the adrenal glands were removed in two stages using the flank approach. The future course of patients with advanced neoplastic disease who are benefited by bilateral adrenalectomy is uncertain, since the regression of the tumor, whenever attained, is not permanent. The intervention is only an aggressive form of palliation for these patients. Hypotensive crises in the immediate postoperative hours may be treated with pressor agents such as arterenol. Generally it is possible to reduce the cortisone dosage to a maintenance level of 50 mg. daily within the first week. Neither diabetes nor hypertension is a contraindication to adrenalectomy if the renal function is not impaired. The intervention is contraindicated in patients with pronounced impairment of the renal function.

FOREIGN

Acta Neurologica et Psychiatrica Belgica, Brussels

53:417-486 (July) 1953. **Partial Index**

Free Disk Hernia. L. Ectors.—p. 417.
*Familial Incidence and Predisposing Factors in Encephalitis of Smallpox Vaccination. G. André-Balisaux.—p. 438.
Tumors of Posterior Fossa with Supratentorial Symptomatoloy. R. Van den Bergh.—p. 472.

Familial Incidence and Predisposing Factors in Postvaccination Encephalitis.—Observations by others have shown (1) the existence of a familial predisposition to neurological or psychic sequelae of exanthemas; (2) the possibility that a new infection may reactivate disturbances seen in the course of a preceding exanthema; and (3) the necessity of taking old craniocerebral traumas sustained in earliest infancy into consideration when interpreting the nervous frailty of certain patients, even though they show no signs of deficit. Similar findings have been reported in patients with postvaccination encephalitic symptoms of neural impairment. The family antecedents and electroencephalographic tracings of the healthy brothers and sisters of patients with postvaccination encephalitis were therefore studied in an effort to discover subclinical signs of cerebral impairment capable of causing future disturbance. The first family consisted of the father, aged 35, healthy; the mother, 32, delicate, slightly nervous, with a tendency toward anemia; and three sons, 13, 10, and 9 years old. The eldest son had encephalitis following smallpox vaccination at the age of 9; marked sensitivity to hyperpnea was the only residual electroencephalographic disturbance. The second son was studied during an attack of encephalitis. The first tracing, made 14 days after vaccination and 10 days after the first signs of encephalitis, showed pronounced slowing and numerous delta waves with clear aggravation during hyperpnea. The second tracing, made 10 days later, was still disturbed, but the third, made one month after the onset of encephalitis, was normal for a child of the patient's age and remained stable during hyperpnea. The third son had never been vaccinated and had normal tracings. The second family was composed of healthy parents, a sister, and four brothers, aged from 20 to 30 years. The oldest brother and the sister were not examined. Two of the other brothers had no neurological complications in the course of vaccination, but presented electroencephalographic abnormalities that could be considered signs of clinically silent changes in the nervous system. The third had meningoencephalitis after revaccination at the age of 22. Electroencephalographic examination showed changes similar to those found in his brothers, but very much more pronounced. These findings indicate the existence both of a familial predisposition to cerebral reactions and of predisposing factors, such as psychic and somatic trauma or toxic infection. Conjunction of the predisposition and the predisposing factors would produce sensitization of the central or peripheral nervous system resulting in a "neuroallergic" reaction. Electroencephalography is apparently valuable as a method of detecting subclinical anomalies favoring the appearance of postvaccination encephalitic complications in predisposed families.

Archives of Disease in Childhood, London

28:247-342 (Aug.) 1953. **Partial Index**

Crossed Laterality: Study in Its Significance and Treatment in Ordinary School Life. R. A. H. Pearce.—p. 247.
Accidental Poisoning in Childhood. J. O. Craig and M. S. Fraser.—p. 259.
Estimation of Blood Pressure in Childhood with Special Reference to Choice of Standard Cuffs. H. Sainsbury.—p. 268.
Fourteen Cases of Idiopathic Myocarditis in Infants and Children. H. Williams, R. N. O'Reilly and A. Williams.—p. 271.
Left Auricular Enlargement in Endocardial Fibro-Elastosis. J. L. Freer and W. J. Matheson.—p. 284.
Acute Isolated Myocarditis in Newborn Infants. J. M. Drennan.—p. 288.
Thirty-Eight Cases of Haemolytic Disease of Newborn. Z. Shamir and J. Gurevitch.—p. 292.
Renal Thrombosis Complicating Pink Disease: Cure by Nephrectomy. W. G. Q. Mills and T. K. Owen.—p. 300.
Haemorrhagic Infarction of Kidney Treated by Nephrectomy. C. D. Clark and J. D. Pickup.—p. 302.

Australian and New Zealand J. Surgery, Sydney

23:1-80 (Aug.) 1953

Talcum Powder Granuloma. N. Johnson.—p. 1.
Malformations of Anus. F. D. Stephens.—p. 9.
Mechanism of Circumflex and Other Nerve Injuries in Dislocation of Shoulder, and Possible Mechanism of Nerve Injuries During Reduction of Dislocation. G. W. Milton.—p. 25.
Dysgerminoma of Ovary. F. Forster.—p. 31.
Ano-Rectal Suppuration. E. S. R. Hughes.—p. 41.
*Vagal Body and Its Tumour. J. H. W. Birrell.—p. 48.
Surgical Pathology of Carcinoma of Lung. J. Borrie.—p. 55.
Value of Exposure in Local Burns Therapy. J. T. Hueston.—p. 63.
Gall-Stone Ileus. R. H. Stanistreet.—p. 73.
Intestinal Obstruction Due to Impacted Gall-Stones. L. Janes.—p. 77.

Vagal Body and Its Tumor.—The patient, a 36-year-old woman, complained of a swelling high up in the right side of her neck which had first appeared 11 years previously. A soft rubbery swelling was observed in the right lateral wall of the pharynx, and this had pushed the wall of the oropharynx almost to the midline of the palate. On the outer surface of the neck a similar swelling, continuous with that in the pharynx, presented between the angle of the mandible and the mastoid process. The tumor was deep to the sternocleidomastoid muscle and showed no fluctuation. Exploration of the tumor was carried out through an incision parallel to the anterior border of the sternocleidomastoid muscle after which the muscle was divided transversely at its upper insertion. The tumor was covered by a network of blood vessels and this extreme vascularity made its exposure difficult. A cavity the size of a large hen's egg, through which the carotid artery ran a sinuous course, remained after the removal of the tumor. The patient's postoperative course was uneventful except for a right recurrent laryngeal nerve palsy and paralysis of the right half of the tongue. At the time of writing this report the patient remained well. On pathological examination of the removed tumor it was classified as a small mass of hyperplastic tissue closely resembling the carotid body in its structure, and situated in or near the ganglion nodosum of the vagus nerve. The normal vagal body is a somewhat diffuse lobulated mass of vascular cellular tissue; its structure and innervation has been shown to be similar to that of the carotid body. The vagal body is grouped with the carotid body and similar masses of tissue as chemoreceptor bodies, which are not considered to have any relation to the chromaffin system. The general close histological resemblance of the tumor to the normal vagal body in conjunction with the encapsulation of the tumor, paucity of mitoses, and apparent benign clinical course were sufficient to make the author cautious of accepting any claims of neoplasia. As far as can be ascertained the present case is the fourth of a vagal body tumor to be reported in the literature.

Boletín Médico del Hospital Infantil, México

10:103-234 (April 1) 1953. **Partial Index**

Enzymatic Activity of Duodenal Contents in Children with Third Degree Malnutrition. F. Gómez, R. Ramos Galván, J. Cravioto and others.—p. 106.
Some Considerations on Pathogenesis of Brucellosis. F. López Clares and A. Pérez Ramírez.—p. 160.
*Mucoepidermoid Carcinoma of Parotid Gland: Case in Girl 8 Years Old. H. Salce, A. Aguirre, M. Salas and others.—p. 166.

Mucoepidermoid Carcinoma of Parotid Gland.—Mucoepidermoid carcinoma of the parotid gland is very rare in children. Five cases have been reported in the American literature. The case reported in a girl 8 years old is the first reported in the Mexican literature. The parotid tumor grew slowly for one year. It was painless at first and later became very painful and opened in two fistulas. Partial resection of the parotid gland was made. Histological study of the surgical specimen showed a mucoepidermoid carcinoma with formation of a large cyst and of a large number of small cysts. The patient was in satisfactory condition after the operation. However, in less than a month she complained of the appearance of a hard nodule in the sternocleidomastoid muscle. A biopsy proved that the nodule was of the same type as the tumor previously removed. Total paratidectomy with radical dissection of the tissues of the neck, in a block, was made.

The tumor included numerous small cysts. Metastases were identified in the lymph nodes of the lateral chain of the neck. Local irradiation was given in the postoperative period. Only a few months after the operation the patient had gained some weight. Sequelae from the operation and the irradiations are peripheral facial paralysis and local edema. A prognosis cannot be ventured, because of the lack of experience with tumors of this type in children.

British Journal of Cancer, London

7:157-282 (June [No. 27]) 1953. **Partial Index**

Significance of "Early Diagnosis" in Breast Cancer: Study of Some Common Usages of the Term. L. Kreyberg.—p. 157.
Chronic Iodine Deficiency as Cause of Neoplasia in Thyroid and Pituitary of Aged Rats. F. Bielschowsky.—p. 203.
Hormonal Background of Ovarian Experimental Tumourigenesis in Guinea-Pig. R. Iglesias, E. Mardones and A. Lipschutz.—p. 221.
Radiobiology of C3H Mouse Mammary Carcinoma: Comparative Radiosensitivity of Tumour Prior to Implantation and of Established Tumour in Situ. A. Cohen and L. Cohen.—p. 231.
Behaviour of Ascites Tumour Cells in Vitro and in Vivo. I. Lasnitzki. —p. 238.
Distribution of Radioactivity Following Administration of Sulfur 35-Labelled Disodium Fluorene-2, 7-Disulfonate in Mice Bearing Transplantable Stomach Carcinoma. M. F. Argus.—p. 273.

British Journal of Radiology, London

26:441-496 (Sept.) 1953. **Partial Index**

Gastro-Oesophageal Regurgitation and Oesophageal Hiatus Hernia with Special Reference to Differential Diagnosis of Angina Pectoris. B. Donnelly.—p. 441.
Radiation Dosimetry with Scintillation Detectors. E. H. Belcher.—p. 455.
New Method of Treatment for Arthritis. N. S. Finzi.—p. 488.
Osteitis Condensans Ilii. C. F. Hutton.—p. 490.

British Medical Journal, London

2:521-578 (Sept. 5) 1953

Bronchial Carcinoma: Incidence and Aetiology. R. Doll.—p. 521.
Some Apparent Anomalies of Potassium Metabolism. I. W. MacPhee. —p. 528.
Gastric Ileus Due to Potassium Depletion After Gastro-Enterostomy. J. S. Logan.—p. 532.
Paroxysmal Paralytic Myoglobinuria. S. D. Elek and H. F. Anderson. —p. 533.
Splenectomy in Three Cases of Myelophthisic Anaemia. C. Merskey and O. E. Budtz-Olsen.—p. 537.
Value of Primidone in Epilepsy. C. W. M. Whitty.—p. 540.
Paraplegia Due to Paget's Disease (Osteitis Deformans). R. G. Robinson. —p. 542.
Recurrent Gall-Stone Ileus. J. A. Macfarlane.—p. 544.

Bull. World Health Organ., Geneva

9:171-310 (No. 2) 1953. **Partial Index**

Preliminary Studies of Iodine Metabolism in Patients from Area of Endemic Goitre. J. B. Stanbury.—p. 183.
Autoradiographic Study of Simple Goitre. S. Taylor.—p. 197.
Studies on Stability of Iodine Compounds in Iodized Salt. F. C. Kelly. —p. 217.
Preparation of Iodized Salt for Goitre Prophylaxis. J. C. M. Holman. —p. 231.
History of Prevention of Endemic Goitre. O. P. Kimball.—p. 241.

Chirurg, Berlin

24:385-432 (Sept.) 1953. **Partial Index**

*Additional Studies on Differences of Behavior of Temperature and Pulse Between Patients with Postoperative Thromboembolism and Those Operated on Without this Complication. H. Peters, H. Döring and P. Seulberger.—p. 385.
Technique and Value of Portography for Diagnosis of Portal Hypertension and Its Treatment. E. Ungeheuer.—p. 394.
Operative Trauma of Inferior Vena Cava and Problem of Air Embolism. S. Petković.—p. 399.

Temperature and Pulse of Surgical Patients With and Without Postoperative Thromboembolism.—An abnormal drop in temperature and discrepancies between temperature and pulse were previously described by the authors as a characteristic sign of threatened thromboembolism. The incidence of these symptoms was reported in 288 surgical patients with postoperative thromboembolism and in 288 patients without this complication. Absolute values of measurements of temperature and pulse before the surgical intervention and during the postoperative course in these two groups of patients are reported and compared in the present paper. Results showed that high temperature and high pulse rate in patients with an uncomplicated postoperative course corresponded with the sympathetic phase that is elicited exclusively by the operative stimulus. The increase of the sympathetic tonus, therefore, induced a simultaneous increase of temperature and pulse rate. Patients with threatened thromboembolism already presented a greater lability of the pulse before the operation than those in whom there is no threat of thromboembolism. The impending surgical intervention as well as other psychic excitement during the day preceding the operation are to be considered as a stimulus which may increase the pulse rate in patients with a labile autonomous nervous system. A high increase of temperature but not of pulse rate in the sympathetic postoperative phase characterized the patients less than 60 years of age with threatened thromboembolism. Patients over 60 with threatened thromboembolism did not show a high increase of temperature in the sympathetic phase. There were no differences in the pulse rate between the patients in the sympathetic phase. A high pulse rate with very low temperature in the parasympathetic phase strongly indicated threatened thromboembolism. Temperature and pulse depend on the function of the central-autonomous nervous regulation apparatus. This apparently is disturbed in patients with threatened thromboembolism.

Clinica Terapeutica, Rome

5:1-99 (July) 1953. **Partial Index**

*Gangliоplegics in Essential Hypertension. C. Bartorelli and R. Rumolo. —p. 3.
*Ion-Exchange Resins. I. Pannacciulli.—p. 40.

Gangliоplegics in Essential Hypertension.—Hexamethonium salts were given intravenously, intramuscularly and orally to 60 patients with essential hypertension. The systolic and diastolic pressures dropped in all the patients. The hypotensive effect was correlated with the route of administration. It was the same when hexamethonium was given intramuscularly or intravenously to patients in the lying position. There was a greater pressure fall when the drug was given intravenously to patients in the standing position, but the hypotensive effect lasted longer when it was administered intramuscularly. The individual response to the drug varied, especially when it was given orally. Orthostatic collapse is the major side-effect of hypotensive therapy, and it is commonest when the parenteral route is used. It does occur also after oral administration of the drug. Side-effects are more frequent after oral administration, and they affect mainly the digestive tract. Severe constipation is the commonest. In many cases this side-effect may be prevented with laxatives or neostigmine (Prostigmin) although these may interfere with the hypotensive therapy. Experimental and clinical data indicate that the cerebral, coronary, and renal circulations are not impaired if the hexamethonium-induced hypotension is not too pronounced. Great caution should be taken before instituting this therapy in patients with arteriosclerotic or other type of vascular lesion. Caution should also be used in patients with diabetes and in pregnant women. In the former the therapy potentiates the hypoglycemic effect of insulin and in the latter the fetus may reabsorb some of the hexamethonium from the amniotic fluid, since the placenta barrier is permeable to this gangliоplegic. This therapy is contraindicated in patients with angina pectoris, cardiac infarct, and renal complications.

Ion-Exchange Resins.—The author reports on the ion-exchange resins and their importance in medicine. The anion-exchange resins have given good results in the treatment of gastric ulcer and hyperacidity of pregnancy. The cation-exchange resins have greater importance because of their capacity to restrict the absorption of sodium. They are indicated mainly in the treatment of edema if combined with a moderate sodium intake. Good results have been reported in patients with edema due to heart insufficiency, liver cirrhosis, and renal disease. They were also beneficial in pregnant women with eclampsia

and potential edema. Their use has been attempted in patients with hypertension, potassium deficiency due to cortisone therapy, and hyperpotassemia. They should be administered orally in doses of 15 gm. three to four times a day near meals in conjunction with a moderately low sodium intake (2 to 5 gm. daily). The best results are obtained when they are administered in repeated courses of 5 to 10 days with a treatment-free interval of 2 to 3 days between each course. The side-effects of treatment with resins are acidosis, especially in patients with renal insufficiency, potassium deficiency, and severe constipation. Granular casts with traces of albumin have been found by some authors in the urine of persons and animals treated with resins, but since they did not find any organic alteration in the tubules they attributed them to the increased urinary acidity. Tremor and psychic effects may follow administration of resins to patients with liver disease. Sulfonamides, saline purgatives, and salt substitutes should be avoided during administration of resins, and digitalis should be used with caution.

Deutsche medizinische Wochenschrift, Stuttgart

78:1205-1244 (Sept. 4) 1953. **Partial Index**

Lymphogenous Spread of Disease. K. Bingold and W. Trummert. —p. 1205.
Symptomatology of Acute Perforation of Septum. G. Jantzen.—p. 1210.
Pre- and Postoperative Functional Aspect in Intervention on Valves of Left Heart and in Cardiolysis. W. Bolt, H. W. Knipping, H. Valentin and H. Venrath.—p. 1214.
*Treatment of Neurosyphilis with Penicillin. H. J. Dammann and E. Schmidt.—p. 1231.

Penicillin in Neurosyphilis.—In 1950, 12 million units of penicillin G sodium were given in aqueous injections of 200,000 units over a period of 10 days to 29 women and to 19 men with neurosyphilis. Of the 48 patients, 18 had cerebral and cerebrospinal syphilis respectively, 1 had cerebral gumma, 12 tabes, 5 progressive paralysis, 1 syphilitic meningitis, 1 syphilitic atrophy of the optic nerve, and 9 had latent syphilis with positive cerebrospinal fluid. Except for a few, these patients did not receive any further treatment up to 1952 when follow-up examinations were performed on 20 of the 48 patients. Pleocytosis and increase of the total protein values had been reduced within six months after the termination of the treatment in most of the patients, and these values had remained low without further treatment. As compared to results of the first examination six months after the termination of the penicillin treatment, the number of cells was reduced in one additional patient, and reduced total protein values were observed in two additional patients. The stained test that had revealed improvement in 17 patients six months after the termination of the treatment did not show any additional improvement. The reaction of the cerebrospinal fluid to the Wassermann test had within half a year after the treatment become negative in two cases, and within two years in two additional cases. The reaction of the blood to the Wassermann test showed a similar behavior. All the patients stated that they felt better subjectively and that their work capacity was improved. Objective neurological and psychiatric findings were not changed. The authors state that penicillin proved adequate for the treatment of neurosyphilis and metasyphilis. Improvement in the cerebrospinal fluid occurs within the first six months. Normalization of the cerebrospinal fluid within the next one to two years was observed in only a few cases. Comparison of the results obtained with the penicillin therapy in the 48 patients with those obtained in 17 patients who had received combined neoarsphenamine, bismuth, and malaria therapy indicated that the results were of practically equal value. The advantages of the penicillin treatment consist of the simpler application and the much rarer occurrence of complications. The much shorter stay in the hospital required for the penicillin treatment as compared to the combined chemotherapy and malaria therapy is an additional factor in favor of the penicillin treatment. The authors believe that preference should be given to penicillin therapy. Combined treatment with penicillin and bismuth is at present the method of choice.

Journal of Clinical Pathology, London

6:99-172 (May) 1953. **Partial Index**

Separation of Serum Pigments Giving Direct and Indirect van den Bergh Reaction. P. G. Cole and G. H. Lathe.—p. 99.
Diurnal Variation of Serum Iron Level in Erythropoietic Disorders. J. C. S. Paterson, D. Marrack and H. S. Wiggins.—p. 105.
Significance of Blood and Cerebrospinal Fluid Urea Levels Estimated After Death. W. J. Jenkins.—p. 110.
Analysis of Calculi Using Microchemical Methods. P. F. Holt and A. L. Tarnoky.—p. 114.
Comparison of Techniques for Measuring Isoniazid Resistance of Tubercle Bacilli. D. A. Mitchison.—p. 118.
Use and Abuse of Jungmann's Method for Liquefaction of Tuberculous Sputa. K. Anderson, J. A. Hughes and R. Knox.—p. 124.
Encephalopathy Following Administration of Streptomycin and Para-Amino-Salicylic Acid. J. B. Cavanagh.—p. 128.
Tuberculosis as Necropsy Room Hazard. G. S. Smith.—p. 132.
Rhabdomyosarcoma of Breast. R. W. Evans.—p. 140.
Case Surviving Six Months After Traumatic Rupture of Aorta. R. Rodda. —p. 145.
Comparative Sensitivity of Male Toad Pregnancy Test and Friedman Test. G. M. Jeffree.—p. 150.

Journal Obst. & Gynaec. Brit. Empire, Manchester

60:445-604 (Aug.) 1953. **Partial Index**

*The Thyroid Gland and Its Relation to Menstrual Cycle of the Baboon (Papio Ursinus). J. Gillman and C. Gilbert.—p. 445.
*Spread of Staphylococcus Aureus in Maternity Department in Absence of Severe Sepsis. M. Barber, B. D. R. Wilson, J. E. Rippon and R. E. O. Williams.—p. 476.
Value of Vaginal Smear to Gynaecologist. R. M. Graham.—p. 483.
Foetal Risk in Breech Presentation. D. Daley and A. M. Michael. —p. 492.
Tertiary Syphilis of Uterus and Adnexa. M. K. Lawlor and K. S. Rodan. —p. 502.
Bleeding in Placenta Praevia. S. Bender.—p. 508.
Phenomena Correlated with Ovulation as Guides to Appraisal of So-Called Safe Period. W. T. Pommerenke.—p. 519.
Constriction of Umbilical Cord by Amniotic Band: Rare Cause of Intra-Uterine Death. A. S. Duncan.—p. 529.
Ovarian Cysts in Newborn Infant of Diabetic Mother. G. M. Hamilton. —p. 533.
Carcinoma and Tuberculosis of Fallopian Tubes. H. G. Wolskel, V. H. Barnett and M. Symons.—p. 535.
Cerebral Metastases from Cervical Carcinoma. J. D. Andrew.—p. 545.

Relation Between Thyroid and Menstrual Cycle in Baboon.—The thyroids of 10 adult female baboons were completely removed at various stages during the menstrual cycle. The baboons were over 7 years of age, having passed through puberty some four years previously. The cycles of each animal were followed by daily inspection and measurement of the sex skin for at least one year and in some instances for three to four years before thyroidectomy. The rhythmical changes in the perineum, the duration of the component phases of turgescence and deturgescence, as well as the total length of the cycle of the 10 baboons, fell within the normal range. After thyroidectomy the parathyroid glands were carefully dissected out of the thyroid, and were reembedded in the deep fascia of the neck. The possibility that tiny fragments of thyroid tissue remained after surgical ablation could not be discounted. Ten normal female adult baboons over 7 years of age constituted the control series. Disturbances in the menstrual rhythm occurred in the 10 female baboons whose thyroids were removed, which indicates that the thyroid gland is closely connected with the regulation of the normal menstrual cycle. Day-to-day examination of the perineal reactions provided evidence, first, that the removal of the thyroid gland profoundly modified ovarian activity and, secondly, that ovarian function, as reflected by the perineum, ranged from inhibition, associated with suppression of perineal cycles, to interference with ovulation and persistence of estrogen stimulation with irregular perineal cycles. Although the menstrual cycle was disturbed in all baboons whose thyroids were removed, the exact disturbance varied from one baboon to another. From a reconstruction of the events encountered in the endometrium, it was evident that after thyroidectomy a rhythm did occur, albeit strikingly different from that seen in the normal baboon. Attention was drawn to the difficulty of assessing the endocrine function of the ovaries from the structure of the endometrium. In attempts to unravel the complex and variable reactions of the uterus, perineum and

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ovaries in baboons following thyroidectomy, consideration was given to the role of the pituitary gland. Suggestive evidence was available to the effect that derangement of ovarian function observed in such baboons was the consequence of a widespread metabolic disturbance involving not only a modified gonadotrophic activity of the pituitary but also a modified responsiveness of the ovaries to the pituitary hormones.

Spread of Staphylococcus in a Maternity Department.—What determines an outbreak of severe sepsis such as pemphigus neonatorum in a maternity department or infants nursery where Micrococcus pyogenes var. aureus (Staphylococcus aureus) is prevalent? To answer this and other still unsolved problems, an investigation was undertaken, which aimed to ascertain, first, whether strains of M. pyogenes var. of aureus spread from nose to nose in a community in the absence of severe sepsis as readily as when sepsis is present? Secondly, whether all strains of M. pyogenes var. aureus isolated from hospital communities are of potentially equal virulence and, if not, can this be demonstrated in the laboratory as claimed by Knott and Blaikley? The department studied had had no severe cases of staphylococcic sepsis for a considerable time, although cases of mild conjunctivitis were common. Over a period of four months swabs were taken from the anterior nares of mothers on admission and on discharge and of babies on discharge. Similar swabs were taken from the nursing and the medical and domestic staff on three occasions during the investigation. A number of swabs were also taken from mothers during the course of their stay and from various samples of dust and bedding. There seemed to be evidence that certain strains of potentially pathogenic staphylococci were spreading round the department. Over half the nurses were nasal carriers of penicillin-resistant M. pyogenes var. aureus and the predominating phage-type was 52A. Many mothers in the short period of 10 days apparently picked up penicillin-resistant strains of M. pyogenes var. aureus of phage-type 52A. The noses of 75% of the babies became colonized with M. pyogenes var. aureus; in nearly 90% of carriers the strain isolated was penicillin-resistant and in a third of the cases it was phage-type 52A. Study of the type of strains isolated from babies, mothers, and nurses indicates that the babies picked up staphylococci more readily from the nurses than from their mothers. No definite answer can be given to the question of why there was no severe sepsis, despite the fact that it must be assumed that potentially virulent strains of penicillin-resistant M. pyogenes var. aureus were spreading. From the bacteriological point of view it is bad to herd babies together in a ward, into which a nurse goes to attend to them one after another. In the department here studied there was not even running water in the baby wards, so that in order to wash between handling each baby the nurse had to leave the room. It was not her practice to change her gown between attending to each infant. A rearrangement of maternity departments with separate units for each mother and baby seems desirable. Recent observations have shown that both the total nasal carriage rate of M. pyogenes var. aureus and the incidence of resistant strains are much lower among babies born in the comparative privacy of their own homes than among babies born in hospitals.

Lancet, London

2:461-524 (Sept. 5) 1953

To the Newly Graduated: Valedictory Address. S. Smith.—p. 461.
Basic Science: Some Observations in the United States. D. C. Sinclair. —p. 463.
Back to Front? Possible Reorientation of Medical Curriculum. A. C. Dornhorst.—p. 468.
Teaching of Social and Preventive Medicine: Some Recent Developments. J. Pemberton.—p. 469.
Models in Medical Teaching with Note on Use of New Plastic. L. H. Hamlyn and P. Thilesen.—p. 472.
On Case-Reports. R. Whitehead.—p. 475.
Development of an Anaesthetic Service Overseas: Organisation and Teaching. L. T. Scott.—p. 478.
Recording Progress in Dissecting-Room: Visual Display Method. D. C. Sinclair and H. D. Darcus.—p. 482.
"How-to-do-It" Teaching Film: An Experiment in Its Use. P. N. Cardew, W. H. Hughes and P. Collard.—p. 484.

Medical Journal of Australia, Sydney

2:41-80 (July 11) 1953. **Partial Index**

*Fluorine and Dental Caries. A. B. P. Amies and P. Pincus.—p. 41.
Lead Hazard in Aviation Industry. F. S. Parle.—p. 47.
Granuloma Inguinale. S. D. Watsford and L. W. Alderman.—p. 50.
Prevalence of an Abnormal Breathing Mechanism in Cases of Respiratory Allergy. B. Gandevia.—p. 52.
Bilateral Carcinoma of Breast. J. M. Yeates.—p. 54.
Another Record of Human Diphyllobothrium in Australia. D. F. Sandars. —p. 55.
Renal Carbuncle: Report of Five Cases, with Some Remarks on Aetiology and Treatment. T. F. Rose.—p. 58.
Lead Intoxication in Three Families. A. Bridge.—p. 62.

Fluorine and Dental Caries.—Amies and Pincus discuss fluoridation of water supplies as a measure for prevention of caries. In discussing certain biochemical aspects of fluorine in water and certain articles of diet, Amies and Pincus direct attention to the influence of the drinking of tea on the intake of fluorine in Australia and New Zealand. As an example, they cite Dunedin, New Zealand, where the municipal water supply contains 0.05 ppm of fluorine. From ordinary infusions of tea (without milk) made with this water, it was calculated that tea could contribute from 0.45 to 0.93 mg. of fluorine per day when the tea ration allowance was 8.1 gm. per day. This would indicate that the average person can obtain approximately 1 mg. of fluorine per day from tea. This amount has been suggested as the optimal intake of fluorine for preventive effects. A person who is a heavy consumer of tea without milk, therefore, cannot afford to take in more fluorine than that already provided by tea, without exceeding the suggested optimum. Current investigations in the United States have demonstrated a temporary partial control of dental caries in young children by the artificial fluoridation of municipal water supplies. Nothing more can be claimed at present. Adequate dental treatment and oral hygiene continue to be essential. Investigations in England in areas in which fluorides occur naturally in water revealed that the caries incidence in 12-year-old children who consumed such drinking water was less than that in control groups; but a survey of 15-year-old children indicated an equal incidence of caries in both groups. This merely demonstrated a three year lag. It is also pointed out that fluorine is a powerful inhibitor of enzymes and a bactericidal agent for some bacteria. The actual chemical form in which sodium fluoride exists after addition to municipal water supplies has not been determined; its physiological ability to be assimilated may be of a different order than that of fluorine occurring naturally in water. The cumulative storage of fluorine in the skeleton and the serious effects of toxic fluorosis have been noted in recent years. The difficulty of statistically assessing the incidence of caries in young children is discussed.

2:81-120 (July 18) 1953

*Regional Non-Bacterial Suppurative Lymphadenitis and Its Relationship to "Cat-Scratch Disease." J. I. Tonge, J. A. Inglis and E. H. Derrick.—p. 81.
Cerebral Astrocytic Gliomata, with Report of Case. I. J. Hunter.—p. 85.
Use of Paraldehyde in Alcoholic Delirium Tremens. D. G. Steyn.—p. 91.
Summary of All Cases of Ante-Partum Haemorrhage in Public Section of Brisbane Women's Hospital During Period from July 1, 1951, to June 30, 1952. J. F. Dunkley and R. Thatcher.—p. 93.
Air Evacuation of Casualties in Korean War. N. M. Kater.—p. 94.
Continuous Immobilization of Joints in Rheumatoid Arthritis. M. Kelly. —p. 95.

Regional Lymphadenitis and "Cat Scratch Disease."—During the last two years nine adults and six children with a peculiar regional nonbacterial suppurative lymphadenitis were studied in Queensland. The clinical behavior of these 15 patients and the microscopic detail of the affected glands presenied a striking similarity to the lymphadenitis occurring in patients with "cat scratch disease." Of 10 patients from whom a reasonably complete history was obtained, 6 gave a history of contact with cats, and of these, 3 stated that they had been scratched or bitten not long before the onset of the lymphadenitis. All three patients on whom an intradermal test was carried out with the "cat scratch" antigen supplied from London gave a positive reaction. Thus the authors believe that the condition observed in Queensland is identical

with the disease described as "cat scratch disease" in America, England, and France. The disease is thought to be caused by a virus of which the cats may act purely as passive carriers. There was no noticeable response of the patients either to sulfonamides or to penicillin, but recovery occurred without sequelae. Although the disease will follow a benign course in most of the cases, there is evidence to suggest that the condition may not necessarily be always benign or localized in character.

Minerva Ginecologica, Turin

5:333-380 (May 31) 1953. **Partial Index**

Histochemical Studies on Polysaccharides of Adrenohypophysis and Considerations on Their Possible Relationships with the Gonadotropic Function. V. Palla.—p. 333.
*Megaloblastic Anemia of Pregnancy: Pathogenetic Study and Personal Contribution. G. Piozzi.—p. 347.
Genital Carcinoma in Elderly Women: 1,169 Cases in Women Over 60. P. Paracchi and L. Luciani.—p. 355.

Megaloblastic Anemia of Pregnancy.—The problem of megalobastic anemia developing during the last months of pregnancy has not been solved. Since the fetus accumulates iron during its intrauterine life and thus alters the systemic iron balance of the mother, there may be a tendency, even if only a potential one, toward a deficiency of iron in the pregnant woman. The constitution of the person must play a great part in this complication. Women who are predisposed to blood diseases have a lesser defensive power against the fetus-placenta toxins which are liberated during pregnancy. Some authors believe that diet alone, even if rich in iron, cannot prevent the onset of anemia in these persons. Lack of vitamins and the action of the estrogens, which are increased during pregnancy, may also be responsible. The changed endocrine balance affects the bone tissue, and these modifications have repercussions on the anatomic and functional balance of the bone marrow. The hemopoietic organs become unable to counterbalance the erythrolysis and erythrocatheresis that are increased during pregnancy, and megaloblastic anemia develops. The author reports on two young women in whom this complication appeared suddenly during the eighth month of pregnancy. Labor began prematurely in both, and blood transfusions were performed. Liver extracts combined with vitamin B_{12} had poor or no effect, but there was a good response to massive doses of folic acid and iron and the blood picture of both patients was much improved. Although blood transfusions and other therapies have improved the prognosis of megaloblastic anemia of pregnancy, its pathogenesis still remains obscure.

Minerva Pediatrica, Turin

5:445-488 (June 30) 1953. **Partial Index**

Chronic Intestinal Intussusception Due to Lymphosarcoma of Ileum Associated with Fibrocaseous Tuberculosis of Mesenteric Lymph Nodes. P. L. Amiotti and B. Possenti.—p. 445.
*Incidence of Tumors in Families of Children with Leukemia. P. L. Amiotti.—p. 449.
Findings and Considerations on Some Cases of Tumors in Children Hospitalized During Last 15 Years in the University of Naples Pediatric Clinic. L. Auricchio and G. Murano.—p. 451.

Cancer in Families of Children with Leukemia.—The author investigated the relationship between malignant tumors and leukemia. He analyzed the genealogical tree of 75 children with leukemia treated at the Gaslini pediatric clinic from 1942 to 1952 and of 75 children who did not have the disease. He found one case of cancer in the family of nine children with leukemia and two cases in the family of one child. Cancer was never present in the parents of these children. It was found in seven of the paternal and four of the maternal grandparents. The incidence of neoplasms was higher in the families of the 75 control children, with one case of cancer in the family of 16 of them, two cases in the family of one, and three cases in the family of one. Cancer was found in the father of one child and in 13 of the paternal and 7 of the maternal grandparents of these children.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

97:1817-1884 (July 11) 1953. **Partial Index**

Internal and Psychosomatic Medicine. G. F. van Balen and G. A. Lindeboom.—p. 1823.
*Blood Pressure in Patients with Steatorrhea. C. D. de Langen.—p. 1830.
Fatal Subprimary and Postprimary Tuberculosis in Rotterdam During 1951 and 1952. M. Straub.—p. 1832.
Experiences with Maurer's Open Treatment of Tuberculous Cavities. A. M. Hendriks.—p. 1837.
Transurethral Removal of Low-Seated Ureteral Calculi Under Paracystoscopic Control. C. L. A. Grove.—p. 1845.
Benign Lymphoreticulosis as Cat Scratch Disease. H. B. G. Breijer and R. Gispen.—p. 1849.

Blood Pressure in Patients with Steatorrhea.—De Langen investigated the blood pressure in patients with sprue, since Salvesen, in determining the blood pressure of 84 patients with idiopathic or symptomatic steatorrhea, had observed that nearly all had subnormal blood pressure and that the mean pressure in all was considerably below that of a group of healthy persons of the same ages. De Langen's case material differed from that of Salvesen, since, among 136 patients with steatorrhea studied by him, there were 102 with tropical sprue. Salvesen apparently had not had a single patient with tropical sprue. Despite this difference, however, de Langen was able to confirm that his patients, like those of Salvesen, had low or very low blood pressure. Salvesen had suggested that hypotension might be due to the fact that these patients have a disturbance in the absorption of a substance, probably a lipid, which is essential for the maintenance of an adequate blood pressure. De Langen, however, suggests that the hypotension is not the result of the steatorrhea but rather that the sprue syndrome develops as the result of a circulatory deficiency of the intestinal wall.

Nordisk Medicin, Stockholm

50:1149-1182 (Aug. 20) 1953. **Partial Index**

Urinary Incontinence in Women. A. Ingelman-Sundberg.—p. 1149.
Is Cesarian Section Method of Choice in Transverse and Oblique Positions at Term? E. Aschan and O. Kinnunen.—p. 1152.
Rat Ovary Hyperemia Test as Pregnancy Reaction. W. Lundin.—p. 1155.
Water Metabolism and Menstrual Cycle. B. Friis-Hansen, B. Ibsen and H. Poulsen.—p. 1157.
Potassium Excretion in Urine During Water Test. E. Ryssing.—p. 1158.
*After-Examination of 150 Patients with Exophthalmic Goiter Following Subtotal Thyroidectomy. E. Dollerup, C. J. Hansen and B. Mølgaard.—p. 1161.
Duration of Tuberculin Allergy After BCG Vaccination in Persons Isolated in Institutions. O. Wasz-Höckert and M. Donner.—p. 1166.
Pneumoperitoneum-Disputed Form of Collapse Treatment in Pulmonary Tuberculosis. G. Forestier.—p. 1168.

Follow-Up of Patients with Exophthalmic Goiter Following Subtotal Thyroidectomy.—Seven postoperative deaths occurred among 227 patients treated with subtotal thyroidectomy after preoperative diiodotyrosine treatment. Of the 33 who sent information by letter on the follow-up from 1 to 10 years after the operation, only three reported inability to carry on their daily work. Dollerup and his associates found the results good in 94% of the 150 patients examined in the hospital, with 28.7% fully recovered, 46% with full ability to work and normal metabolism and slight residual symptoms, and 19.3% better able to work than before the operation; in 6% the capacity for work was reduced and there were marked subjective and objective symptoms. Shorter duration of the disease before operative treatment seemed to affect the outcome favorably. Of the total 51 with cardiac symptoms on the follow-up, 41 had normal capacity for work; cardiac symptoms were noted in only 27 of the 39 who had cardiac symptoms before operation. True relapse occurred in 4%.

Tubercle, London

34:205-232 (Aug.) 1953

Principles and Results of Training and Employment at Papworth. O. Clarke.—p. 206.
Observations on Radiological Appearances of Undiagnosed Bronchiectasis. N. Wynn-Williams.—p. 212.
Tension Cavitation at Site of "Healed" Tuberculous Primary Focus: Case Report. J. D. P. David.—p. 217.
Case of Self-Mutilation Presenting as Haemoptysis. B. Mann.—p. 220.

BOOK REVIEWS

Medical Schools in the United States in Mid-Century. By John E. Deitrick, M.D., and Robert C. Berson, M.D. Cloth. $4.50. Pp. 380, with 14 illustrations. McGraw-Hill Book Co., Inc., 330 W. 42nd St., New York 18; 95 Farringdon St., London, E.C.4, 1953.

This volume constitutes the report of the Survey of Medical Education, which was organized in 1947, sponsored, and financed by the American Medical Association, the Association of American Medical Colleges, and the W. K. Kellogg Foundation. It is a factual self-analysis and evaluation of medical education in the United States at mid-twentieth century, based on a survey of 41 carefully selected representative institutions. Conclusions are based on facts and opinions obtained from deans, faculties, and medical students and represents an authoritative current evaluation of medical education, its leadership, function, and finances in the United States. The increasingly complex nature and ever-widening scope of responsibilities and activities of today's medical school are well portrayed and analyzed. Modern medical school functions are indicated to be education, research, and service, so interwoven in most instances that the costs of medical education have not been clearly differentiated from the research and service aspects. The dangers to medical education itself of overemphasis of either research or service activities are clearly implied and the necessity of maintaining a proper balance of these activities emphasized.

Medical school finances are examined in detail, and an analysis is made of the funds involved and how they are spent. Medical schools in operation are evaluated from the standpoint of administration, medical school-hospital relations, departments, faculty, and student admisison problems. The undergraduate curriculum has been subjected to careful scrutiny, and the responsibilities of medical schools in advanced education and training are discussed at length. The authors have presented "a summing up" in their final chapter that will undoubtedly provoke much discussion among medical educators and others interested in this field. This chapter focuses attention on the following questions: What is medical education? What is a medical school, and what are its responsibilities? Should research be the major goal of a medical school and receive the greatest financal support? What is the goal of the medical school in providing medical care?

It is difficult to separate some phases of education and training, and what different medical schools may do in this regard will vary greatly. Locale, finances, service functions, and many other factors naturally emanating as part of different educational programs present variables that continue to keep medical schools from becoming stereotyped. The size of the school and the complexity of organization may be significant problems but need not transcend quality if all factors are properly adjusted. Tradition and authority will continue to be hurdles to progressive curriculum adjustments until broader perspectives are attained by those interested in medical education and departmental barriers are minimized. Certain trends leading young physicians into a philosophy of dependence rather than independence in leadership are pointed out.

There are useful appendixes evaluating student opinions on college preparation and their medical school impressions, analyzing current medical school administrative problems, outlining the distribution of graduates from four-year medical schools and the distribution of libraries, postgraduate education, and finances. This new survey of medical education, like the Flexner Report that appeared in 1910, will be of value to the medical schools and all those interested in medical education, by stimulating further analysis and advances in this field. Today's problems are vastly different from those in 1910 but, nevertheless, present intriguing challenges. In 1910 the Flexner Report brought about a badly needed revolution in medical education that resulted in placing it on an increasingly high plane over the years. The current report tends to focus the complex problems of education, research, and service in medical education today and makes recommendations that should be seriously considered by medical schools and universities in their efforts to solve them. The volume should be read and thoughtfully analyzed by all who are interested in medical education and its ramifications.

These book reviews have been prepared by competent authorities but do not represent the opinions of any official bodies unless specifically so stated.

Medical Education Today: Its Aims, Problems and Trends. By Joseph C. Hinsey, Director, New York Hospital-Cornell Medical Center, New York City, et al. Edited by Dean F. Smiley, Secretary, Association of American Medical Colleges, Chicago. Paper. $1.50. Pp. 123, with 7 illustrations. The Journal of Medical Education, Association of American Medical Colleges, Rm. 1001, 185 N. Wabash Ave., Chicago 1, 1953.

This is a compilation of papers that appeared in recent issues of the *Journal of Medical Education* dealing with important problems confronting medical schools and educators in this dynamic period of readjustment. The seven articles were written by leaders in the field of medical education and constitute an interesting and timely presentation of the problems confronting medical education with an evaluation of potential solutions. The first paper is the eighth revision of the objectives of undergraduate education as they are conceived by the Association of American Medical Colleges today. It clearly portrays the major aims of undergraduate medical education and endeavors to indicate its limitations. Other papers present the problems of staffing medical colleges in four-year medical schools, problems revolving around the selection of medical students, a presentation of the financial status of medical education, an analysis of the distribution and characteristics of medical college graduates during the period from 1915 to 1940, and a final article presenting the challenges confronting medical education at this time. This volume deserves serious review by all medical educators, college presidents, and members of the profession concerned with the problems of medical education.

More Clinical Sonnets. By Merrill Moore. Cloth. $3. Pp. 72, with illustrations by Edward Gorey. Twayne Publishers, 34 East 23rd Street, New York 10, 1953.

Dr. Moore's latest collection of sonnets can be reviewed by repeating comments that have been made about the author's previous sonnets. The sonnets have been described on various occasions as "magnificent"; as expressing "humor and poignancy" and making for "diverting reading"; as "providing acute insight expressed with wit"; as being "pithy, caustic, comic, tender, penetrating, sad, grim, witty, serious"; and as inviting the reader to "start reading and stop if you can." It can only be added, "For the reader who may have an inhibition, a quick cure resides in this edition."

Introduction to Physiological and Pathological Chemistry. By L. Earle Arnow, Ph.G., Ph.D., M.D., Vice-President and Director of Research, Sharp & Dohme Division of Merck & Co., Inc., West Point, Pennsylvania. Revised with assistance of Marie C. D'Andrea, R.N., B.S., Educational Director, School of Nursing, St. Vincent's Hospital, Indianapolis. Fourth edition. Cloth. $3.75. Pp. 508, with 108 illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1953.

So many textbooks of chemistry for nurses have appeared in the last decade that none would reach its fourth edition if it were not exceptionally good. Like the other three editions, this text is simply written, copiously illustrated, and pointed to the interests of student nurses. The major changes from previous editions are deletion of directions for laboratory experiments (to be published in a separate manual) and instructions on the removal of stains from clothing, and addition of separate chapters on nuclear reactions and atomic energy, on agents used in chemical warfare, and on the chemistry of blood. Throughout this book the material has been brought

up-to-date; for example, cortisone, corticotropin, and cyanocobalamin (vitamin B_{12}) are discussed. The printing is of good quality and the binding is sturdy, but the highly glazed paper, which may have been necessary for the illustrations, is hard on the eyes of readers. All instructors in this field will wish to examine this textbook.

Who Shall Survive? Foundations of Sociometry, Group Psychotherapy and Sociodrama. By J. L. Moreno, M.D. Cloth. $10. Pp. 763, with illustrations. Beacon House, Inc., P. O. Box 311, Beacon, N. Y., 1953.

This book is apparently not a first edition, although no mention of earlier editions is made on the title page. In it the author says someone once asked him, "Why is the first edition of 'Who Shall Survive?' so clumsily written?" to which he replied: "In order to make it clear for all posterity that the book could not have been written but by myself alone." In another place he says some one said to him: "You seem to think that 'Who Shall Survive?' is a book of books, a new bible." Moreno admits that it is a new bible, that it has more ideas packed in one book than a whole generation of books, and adds that actually he has written two bibles. The book is a formidable volume and contains a wealth of information on the subjects of sociometry, psychodrama, and group psychotherapy, intermingled with ideas on philosophy, religion, sociology, and countless other fields of thought. In addition, there is a vast amount of tabulated and statistical data as well as a lengthy bibliography. For those interested in such material and in the broad fields to which they apply or for those who are anxious to learn about some of the feelings and philosophical ideas of the author, the book will be of interest. It is written by the man who has generally been given credit for originating group therapy and psychodrama. So far as priority in the field of sociometry is concerned, Moreno offers as the frontispiece to the book a fragment of the "First Sociometric Plan" in the form of a fragment from the original draft of his letter written in 1916 urging the Austro-Hungarian monarchy to apply sociometry to the community of displaced persons in Mittendorf. Elsewhere in the book he says, "I tried to do through sociometry what 'religion without science' has failed to accomplish in the past and what 'science without religion' has failed to accomplish in Soviet Russia." The future will have to determine whether he has succeeded in achieving this ambitious aim.

Lehrbuch der topographischen Anatomie. Von Anton Hafferl, o. Professor der Anatomie und Vorstand des anatomischen Instituts der Universität Graz. Cloth. 60 marks. Pp. 921, with 664 illustrations. Springer-Verlag, Reichpietschufer 20, (1) Berlin W. 35 (West-Berlin); Neuenheimer Landstrasse 24, Heidelberg; Göttingen, 1953.

This fine book on topographical anatomy is the result of much planning and an extensive survey of the available texts and literature. Although numerous standard works deal with this subject, the author has used a fresh approach, and has succeeded in presenting the common anomalies as well as the so-called normal anatomy. The color plates add appreciably to the clarity with which the structural relationships are depicted. The use of red to denote suture lines is particularly helpful.

The following faults detract but little from the value of this work. The discussion of the relationship of the facial nerve to the parotid gland was especially weak. Greater emphasis should have been placed on the possibilities of the nerve passing between the superficial and deep parotid lobes. Figure 208 on page 250 depicts a most unusual looking thyroid gland. No isthmus is shown, and one lobe seems to merge directly into the other. In this same illustration a pyramidal lobe is shown arising from the upper aspect of the right thyroid lobe. Such an origin is rarely, if ever, noted. Although the embryologic development of the pancreas is admirably treated, there should have been more stress on the fact that the common duct travels through the head of the pancreas. Furthermore, this fact was not brought out in figure 356 on page 454. The cystic duct appears out of proportion in figure 366 on page 474.

The sections on the extremities were very well done. The book is printed in large type, and an attempt has been made to shorten the sentences. The latter feature should prove a boon to those whose reading knowledge of German is not fluent. An extensive bibliography is appended.

Tests and Standards for New and Nonofficial Remedies: Containing Tests and Standards for Nonofficial Drugs and Dosage Forms Which Stand Accepted by the Council on Pharmacy and Chemistry of the American Medical Association on January 1, 1953. Issued by The Chemical Laboratory, American Medical Association. Cloth. $4. Pp. 327, with illustrations. J. B. Lippincott Company, 227-231 S. Sixth St., Philadelphia 5; Aldine House, 10-13 Bedford St., London, W.C.2; 2083 Guy St., Montreal, 1953.

This small volume is a companion to "New and Nonofficial Remedies" from which tests and standards were omitted for the first time this year. To make the volume independent of N.N.R., structural formulas have been included in the individual monographs and trade names of Council-accepted brands have been added. Aside from these changes the work is what used to be section B of the annual editions of N.N.R. Substances covered in this volume are nonofficial dosage forms of official products and drugs not in the "United States Pharmacopeia" or the "National Formulary." Many of the nonofficial drugs are too new to be in the official compendiums, which are published at five-year intervals. Thus, the volume is useful to pharmacists, pharmaceutical manufacturers, purchasing agents, and students of pharmaceutical chemistry. The printing and binding are good.

Multiple Myeloma. By I. Snapper, M.D., Director of Medical Education, Cook County Hospital, Chicago, Louis B. Turner, M.D., Research Assistant in Medicine, Mount Sinai Hospital, New York, and Howard L. Moscovitz, M.D., Resident, Second Medical Service, Mount Sinai Hospital, New York. Cloth. $6.50. Pp. 168, with 43 illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16, 1953.

This excellent monograph is based, for the most part, on the authors' extensive study of 97 cases of multiple myeloma, 41 of which were studied post mortem. The discussion of various aspects of the disease encompasses the experience of the authors and relates it to previous findings in the literature, which is fairly completely reviewed. The text is well written and is liberally supplemented by illustrations that are generally very good. The lithography and format are also commendable. The bibliography and index enhance the book's value, even though the bibliography does not pretend to be complete. The main function of the book is to serve as a definitive treatise on the subject to date. Hematologists will certainly want the book for their libraries, and others will do well to browse through it, because multiple myeloma, by virtue of the multiplicity of its manifestations, may be encountered in almost any specialty. Perhaps the greatest value of the book is to call attention to the fact that multiple myeloma is not at all a rare disease, as evidenced by the ability of the authors to collect 97 cases in one institution in seven years.

United States Government Organization Manual 1953-54. Federal Register Division, National Archives and Records Service, General Services Administration. Revised as of July 1, 1953. Paper. $1. Pp. 734. Superintendent of Documents, Govern. Print. Off., Washington 25, 1953.

Because the activities of the federal government are so closely interwoven in the lives of all citizens, it is only natural that curiosity should arise concerning the structure of this government. The manual of the United States Government Organization is revised each year and is the sort of volume that provides ready reference for anyone interested in the make-up of the government, the activities of the departments, the personnel associated with these departments, and other such information. It should be of interest to almost all citizens but often offers particular interest to special groups, for example, members of the legal profession, physicians, and business men. This volume is well worth the dollar it costs, even if it serves no other purpose than to provide an answer to questions that arise concerning discussions of politics. The entire family will refer to this at some time during the year.

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QUERIES AND MINOR NOTES

STERILIZATION BY DRY HEAT

To the Editor:—*At what temperature should the thermostat of a hot air sterilizer be set and how long should it continue for the sterilization of needles, syringes, small instruments, and rubber gloves?*

H. H. Hancock, M.D., Union, West Va.

Answer.—Clean needles, surgical instruments, and syringes can be sterilized by exposure to dry heat at 160 C (320 F) if the sterilization interval is sufficiently long. Usually, exposure for one hour, after the temperature has been attained, is sufficient. If the sterilizer is overloaded or if the heat must penetrate outer covers such as glass tubes or metal trays, the time should be extended. It is recommended that the temperature of the oven be raised gradually to 160 C to permit adequate heat penetration and to prevent excessive strains on glassware. Rubber goods will not withstand exposure to dry heat at the temperature and interval required for sterilization.

THALAMIC SYNDROME

To the Editor:—*A white woman, aged 44, was suddenly stricken four years ago with severe headache with lateral deviation of the right eye. Lumbar puncture revealed blood in the spinal fluid. Cerebral angiography revealed an aneurysm of the right internal carotid artery in the anterior portion of the circle of Willis. Ligation of the carotid vessel on this side was followed within 24 hours by complete left-sided hemiplegia and unconsciousness. Anticoagulant therapy brought excellent improvement. The patient is ambulatory and doing well, except for slight weakness of left arm and left leg with insignificant sensory changes on the left side. One year ago, she began to complain bitterly of a "waxy" sensation in the mouth. Qualified staff members at a recognized dental school had no explanation but suggested that this was a psychosomatic manifestation. This waxy sensation has been unrelenting. She has no interference with taste sensation, but states that periodically there is a hot feeling in her mouth. She complains of a tingling sensation, which is constant over the lower maxilliary and mandibular divisions of the trigeminal nerve bilaterally. It cannot be relieved by mouth washes or any type of food. Can you suggest any therapeutic approach?*

M.D., Alabama.

Answer.—The persistent symptoms and "insignificant sensory changes on the left side" point to a limited lesion within the ventral posteromedial nucleus of the thalamus on the right. Crossed and uncrossed secondary trigeminal pathways have been traced to this nucleus. This would account for the bilateral symptoms. The lesion is in all probability a gliotic area that arose as the result of anoxemia occurring at the time of rupture of the aneurysm or during the critical period after carotid artery ligation. The lesion of necessity is small, since such a limited portion of the body is involved. No specific treatment can be recommended for this condition, which is known as the "thalamic syndrome." Stellate ganglion blocks with procaine could be tried on the chance that the symptoms that were delayed in onset are caused by a vasospastic phenomenon associated with irritation at the junction of normal neural tissue and the area of glial scarring. If the symptoms increase to the point of becoming unbearable for the patient and drug addiction threatens, major neurosurgical intervention must be contemplated. In this event prefrontal lobotomy could be considered or one of the stereotoxic procedures recently devised by Wycis for interruption of ascending pain pathways in the mesencephalon.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any official bodies unless specifically so stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

SMALLPOX VACCINATION

To the Editor:—*Is it true that giving smallpox inoculations without the prior preparation of the skin with an antiseptic agent is a serious break in sound medical principles? It is felt that the intradermal prickings of an inoculation could be compared to shaving, the pressure of a belt or other clothing, the simple rubbing of the skin unconsciously, or the "sandpapering" of acne scars, where there is no thought of artificially induced infection.*

M.D., Virginia.

Answer.—When the skin is cleansed with acetone or ether in preparation for a smallpox vaccination, the area should be dry before the vaccine is applied. To facilitate speed in vaccinating large groups, nurses or medical assistants usually do the preliminary work. With such an arrangement, the physician is concerned only with the actual vaccination and there is no loss of time. If there are failures to secure successful vaccinations in susceptible persons, the potency of the vaccine should be investigated. Vaccine that has not been stored at a low temperature may have become useless. It would be a serious error to ignore the customary technique for cleansing the skin before the vaccine is applied. There is always the possibility of an infection with staphylococci and streptococci present on the surface of the skin. The inoculation of smallpox vaccine cannot be compared to shaving. Many infections have resulted from the other examples mentioned when an unclean skin was abraded, and the cut of a razor—especially on the upper lip—has led to infections that resulted in death.

ASTHMA AND SILICOSIS

To the Editor:—*Would asthma that occurs for the first time in a 52-year-old granite worker be caused or aggravated by silicosis, second stage? Roentgenograms of the chest four years ago showed no abnormalities and three years ago showed scattered mottled shadows.*

Pierre J. Guilfoile, M.D., Delano, Minn.

Answer.—Asthma occurring for the first time in a 52-year-old person can be aggravated by silicosis. The type of dyspnea caused primarily by silicosis is due to damage of the lung parenchyma and to emphysema. In some persons with silicosis, bronchospasm is induced secondarily. It should also be remembered that a 52-year-old man may have allergic infections or cardiac asthma for the first time. If the patient in question has true asthmatic episodes (relieved by epinephrine or aminophylline), a search for other causative factors should be made by a series of observations such as examination of the sputum for eosinophils and neutrophils, skin tests, and examination for hypertensive, coronary, or syphilitic heart disease.

WORK WITH VIBRATING TOOLS

To the Editor:—*May I have some information on the occupational hazard attendant to the use of a jackhammer over a period of years. I am specifically interested in knowing whether or not any type of nerve damage normally follows the continued use of one of these air compressor hammers.*

M.D., Illinois.

Answer.—A variety of physiological disturbances are attributable to the action of vibrating pneumatic and electric tools. Part of the differences in manifestations are attributable to the speed and amplitude of the vibration. Another difference is related to low temperatures attending some pneumatic tool work. As a rule, the severer conditions result from use of high frequency, low amplitude tools. The major disturbances chiefly involve the fingers and are, or are similar to, Raynaud's phenomenon. For some major tools, of which the jackhammer is one, the most frequent damage involves the soft tissues, appearing as synovitis or tendonitis. In addition, arthritis at any point along the upper extremity may result. Also areas

of bone decalcification may arise in the wrist area. Long nerve neuritis is not a common feature but repeatedly has been described, the ulnar nerve being mentioned oftenest. Apart from the tool itself, other factors contribute, such as the posture while at work. Some mining or quarrying operations may require a prone position, leading to much pressure on the outstretched arms. The hardness of the material being drilled is significant.

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Telford, E. D.; McCann, M. B., and MacCormack, D. H.: 'Dead Hand' In Users of Vibrating Tools, Compensation Medicine **1**: 29 (Feb.) 1946.

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ANGINA-LIKE PAINS

TO THE EDITOR:—*A married woman, aged 26, has had angina-like pains for two years. She had one abortion at four and one-half months of pregnancy, followed by infection of the uterus and adnexa, three years ago. The cause of the abortion is unknown. She is Rh negative. She has one living child, aged 5. Two years ago, the patient had peptic-ulcer-like pains, which were partially relieved by the use of methantheline (Banthine) and Prantal (N,N dimethyl-4-piperidylidene-1,1-diphenyl-methane methyl sulfate). Results of upper gastrointestinal tract studies did not indicate an ulcer; one film showed a J-shaped stomach. For the past six months the pains have been precordial; they are severe, sharp pains that radiate to the upper left arm, stopping at the elbow. The chest pain is not affected by deep breathing or exercise but comes on at rest, while the patient is listening to music or even while she is asleep, thus waking her. Swimming and the lifting of heavy objects do not initiate the pain, and it is not related to eating or hunger. The ulcer type of pain no longer seems to be present. The patient's present distress is not relieved by the use of atropine (1/100 grain [0.6 mg.] given intramuscularly), acetylsalicylic acid, phenobarbital, Donnatal (an elixir containing hyoscyamine sulfate, atropine sulfate, hyoscine hydrobromide, and phenobarbital), antispasmodics, or antacids. The pain is severe for several minutes and then dies down, leaving a dull ache that persists for several hours. On several but not all occasions, it was relieved dramatically by the use of glyceryl trinitrate under the tongue. It commonly occurs while the patient is lying on her back. There is no pyrosis. The patient has psychiatric determinants (a broken home in her childhood), and she continues to have weird dreams. The electrocardiogram is normal. Results of roentgenographic and fluoroscopic examination of the chest are normal. The patient claims she is happily married, and she would like to become pregnant again. At an early age she was kept home from school and in bed for several months. Her athletic activity in school was restricted for a year, and she was told she had "weak lungs." She is highly intelligent and perfectionistic and is usually successful in all endeavors. The local internist is unable to find an organic lesion that could cause this pain. Have you any suggestions?*

M.D., California.

ANSWER.—Despite the seemingly obvious psychic implications of the occurrence of the symptoms on recumbency, the patient's condition probably does not have a psychic basis, nor is it likely that the chest symptoms are cardiac in origin. Although decidedly unusual, it is entirely possible that the pain is due to cholelithiasis. A Graham test should be performed. The possibility of a hiatus hernia cannot be excluded on the basis of a single examination; other types of hernia, such as those involving Morgagni's or Bochdalek's foramen, must also be considered. If none of these tests shows abnormalities, use of a therapeutic regimen that has been beneficial to patients with hiatus hernia should be attempted. This would include the eating of only small meals, avoidance of ingestion of liquids and of assuming the recumbent position for at least two hours after any meal, sleeping in as upright a position as feasible, with the use of two or more pillows or even a hospital bed, and a regime of a liberal bland diet.

HISTOLOGICAL SECTIONS

TO THE EDITOR:—*In* THE JOURNAL *of Sept. 19, 1953, page 257, the physician from the Dominican Republic asked about the time required to get a report on a biopsy specimen. Your answer stresses the making of a section and states that after the section is made the interpretation can be made the same day. The autotechnicon is an expensive complicated machine that moves the tissues through the solutions and, therefore, can process tissues during the night. If one wishes, the tissues can be moved through the same solutions by hand. When the volume of work is sufficient, this machine is of some help in getting sections. However, it is possible to process a piece of tissue and get a section in one day without an autotechnicon. The interpretation of the section and preparation and mailing of the report may take much more time. It seems to me that the physician from the Dominican Republic has no just complaint when he says that it takes as long as seven days to get a report. This can only mean that other reports require less time.*

We have three autotechnicons, and I direct one laboratory where we have no autotechnicon. In this laboratory we put formaldehyde-fixed specimens into acetone over night. The next morning they are put into a second acetone solution and then into chloroform and paraffin (two changes). Sections are made late on this day and thus are obtained 18 hours after the tissue is placed in acetone. Small pieces can be run, cut, and stained in 10 hours or even less. To this time for interpretation and report must be added. There is much more to it than getting sections.

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TO THE EDITOR:—*Possibly the physician from Dominican Republic* (THE JOURNAL, *Sept. 19, 1953, page 257) will find the following method for securing histological sections advantageous. For 24 hour tissue processing a pathologist need buy no equipment more expensive than a half a dozen wide-mouthed stoppered 200 cc. bottles. He can improvise a 55 C paraffin oven with an electric lamp as a heating element; the microtome and microscope are the only expensive necessities.*

Tissues as received in 10% formaldehyde may be left until noon, and can be put into the paraffin by 5 p. m., to be ready for sectioning and staining the following morning. The tissues for examination should be cut less than 4 mm. thick and strung on colored threads or with beads for identification, so they will hang in the upper part of the solutions, supported by the stopper. Tissues obtained by curetting may be similarly strung if placed in gauze bags.

First, the specimens should be placed in alcoholic Bouin's solution, and the bottle placed in the paraffin oven for a half hour. After transfer to isopropyl alcohol (absolute), the specimen should be left for an hour in the oven and in a second alcohol solution for another hour. Then the specimen should be left in toluene in the oven for an hour (until the tissues are translucent), in a second toluene solution for a half hour, then in the paraffin overnight.

The isopropyl alcohol bottles are conveniently used with a layer of $CaSO_4$ granules in the bottom, with an indicator. The time required to change from one solution to another as warned by a timer clock is under 1 minute (5 minutes in all). Where time and skill and training are requisite is in the orientation of tissues in the paraffin blocks, the sectioning, and the mounting on slides. Slides taken from the warm water on which they are floated and flattened can be dried of water, and the paraffin melted for rapid removal by toluene preliminary to staining, by placing the slides on a frame set over an electric lamp for a few minutes.

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